

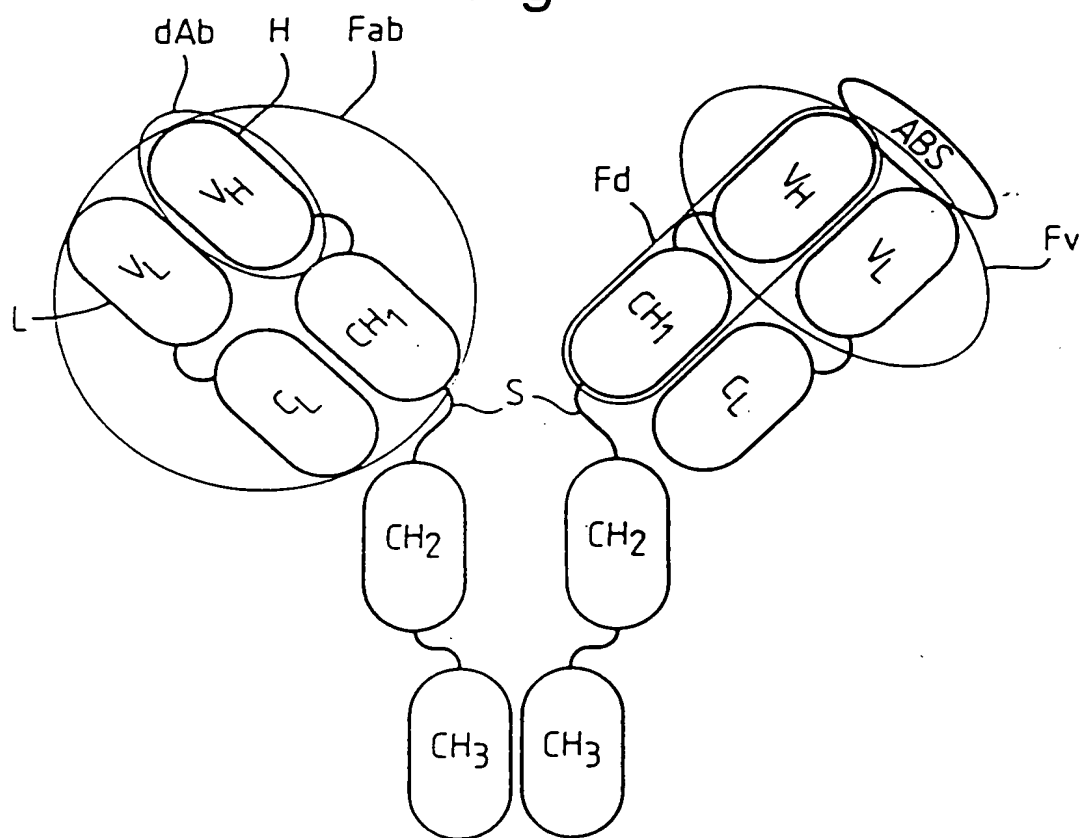
[illegible]

Fig.2 (i).

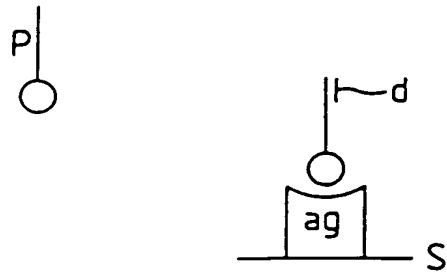


Fig.2 (ii).

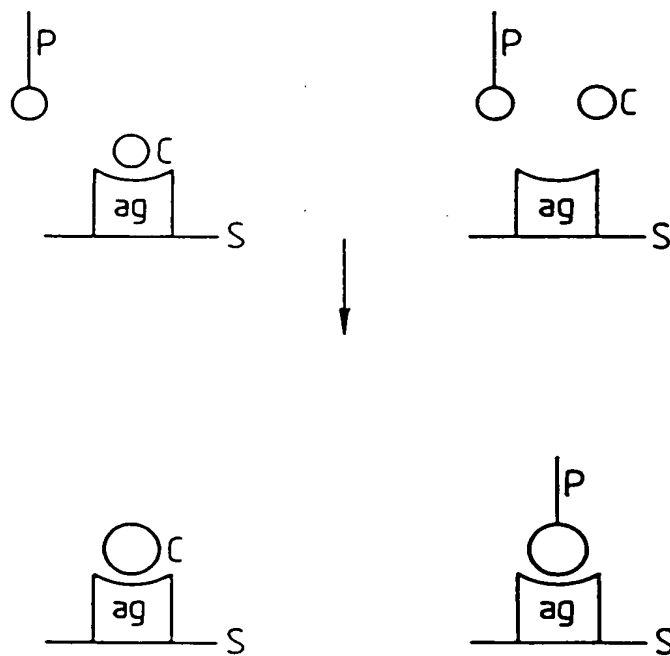
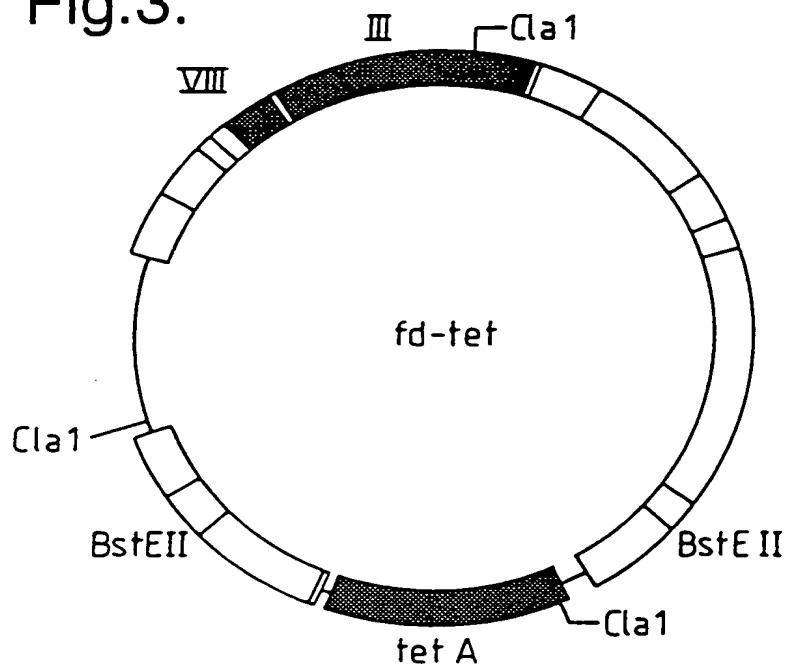


Fig.3.



fd - tet

~

cleave with BstEII

~

fill in with Klenow

~

re-ligate

↓

FDT 6 Bst

~

in vitro mutagenesis (oligo 1)

↓

FDTPs/Bs

~

in vitro mutagenesis (oligo 2)

↓

FDTPs/Xh

(1653)
 Oligo 1 ACA ACT TTC AAC AGT TGA GGA GAC GGT GAC CGT AAG CTT CTG CAG TTG GAC CTG AGC
 GGA GTG AGA ATA (1620)
 (1653)
 Oligo 2 ACA ACT TTC AAC AGT TTC CCG TTT GAT CTC GAG CTC CTG CAG TTG GAC CTG
 (1704)
 Oligo 3 GTC GTC TTT CCA GAC GTT AGT

GENE III

GENE III

SIGNAL
CLEAVAGE SITE

Fig.4 (ii).

(1624)
 A TCT CAC TCC GCT
 Q V Q L Q V T V S S
 B TCT CAC TCC GCT CAG GTC CAA CTG CAG AAG CTT ACG GTC ACC GTC TCC TCA ACT GTT GAA AGT
 PstI BstEII
 Q V Q L Q L E I K R
 C TCT CAC TCC GCT CAG GTC CAA CTG CAG GAG CTC GAG ATC AAA CGG GAA ACT GTT GAA AGT
 PstI XhoI
 (1650)
 GAA ACT GTT GAA AGT

Fig.5.

rbs M K Y L L P T A A
 GCATGCAAATTCATTTCAAGGAGACAGTCATAATGAAATACCTATTGCCTACGGCAGCC
 10 20 30 40 50 60
 SphI
 PelB leader
 A G L L L L A A O P A M A Q V Q L Q E S
 GCTGGATTGTTATTACTCGCTGCCCAACCAGCGATGGCCCAGGTGCAGCTGCAGGAGTCA
 70 80 90 100 110 120
 PstI
 G P G L V A P S Q S L S I T C T V S G F
 GGACCTGGCCTGGTGGCGCCCTCACAGAGCCTGTCCATCACATGCACCGTCTCAGGGTTC
 130 140 150 160 170 180
 S L T G Y G V N W V R Q P P G K G L E W
 TCATTAACCGGCTATGGTGTAAACTGGGTTCGCCAGCCTCCAGGAAAGGGTCTGGAGTGG
 190 200 210 220 230 240
 VHD1.3
 L G M I W G D G N T D Y N S A L K S R L
 CTGGGAATGATTGGGGTGATGGAAACACAGACTATAATTCAGCTCTCAAATCCAGACTG
 250 260 270 280 290 300
 S I S K D N S K S Q V F L K M N S L H T
 AGCATCAGCAAGGACAACCTCCAAGAGCCAAGTTTCTTAAAAATGAACAGTCTGCACACT
 310 320 330 340 350 360
 D D T A R Y Y C A R E R D Y R L D Y W G
 GATGACACAGCCAGGTACTACTGTGCCAGAGAGAGAGATTATAGGCTTGACTACTGGGGC
 370 380 390 400 410 420
 Linker Peptide
 Q G T T V T V S S G G G G S G G G S G
 CAAGGCACCAAGGTCACCGTCTCCTCAgggtggaggcgggttcaggcggagggtggctctggc
 430 440 450 460 470 480
 BstEII
 G G G S D I E L T Q S P A S L S A S V G
 ggtggcggatcgGACATCGAGCTCACTCAGTCTCCAGCCTCCCTTTCTGCGTCTGTGGGA
 490 500 510 520 530 540
 SacI

6547459 " 5247459 " 6547459

Fig.5 (Cont).

E T V T I T C R A S G N I H N Y L A W Y
GAAACTGTCACCATCACATGTCGAGCAAGTGGGAATATTCACAATTATTTAGCATGGTAT
550 560 570 580 590 600

Q Q K Q G K S P Q L L V Y Y T T T L A D
CAGCAGAAACAGGGAAAATCTCCTCAGCTCCTGGTCTATTATACAACAACCTTAGCAGAT
610 620 630 640 650 660

VKD1.3

G V P S R F S G S G S G T Q Y S L K I N
GGTGTGCCATCAAGGTTTCAGTGGCAGTGGATCAGGAACACAATATTCTCTCAAGATCAAC
670 680 690 700 710 720

S L Q P E D F G S Y Y C Q H F W S T P R
AGCCTGCAACCTGAAGATTTTGGGAGTTATTACTGTCAACATTTTGGAGTACTCCTCGG
730 740 750 760 770 780

Myc Tag (TAG1)

T F G G G T K L E I K R E O K L I S E E
ACGTTCCGGTGGAGGGACCAAGCTCGAGATCAAACGGGAACAAAACTCATCTCAGAAGAG
790 800 810 820 830 840

XhoI

D L N * *

GATCTGAATTAATAATGATCAAACGGTAATAAGGATCCAGCTCGAATTC
850 860 870 880

EcoRI

666101-6/47460

Fig.6.

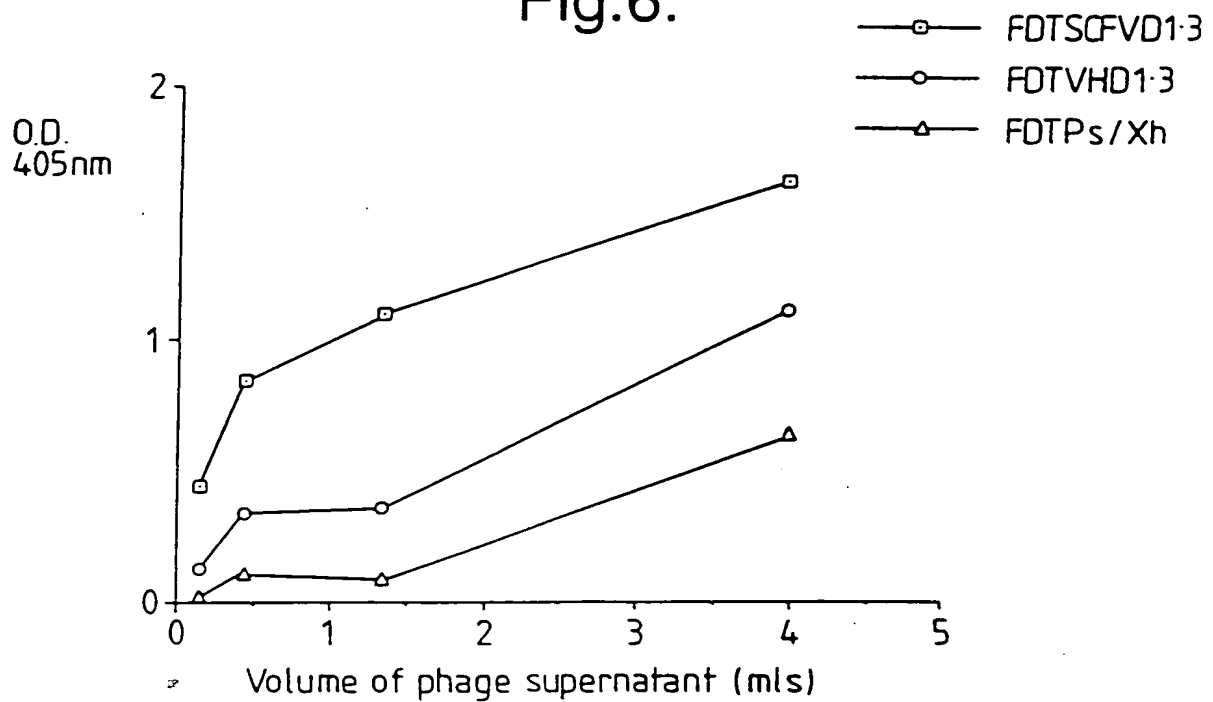
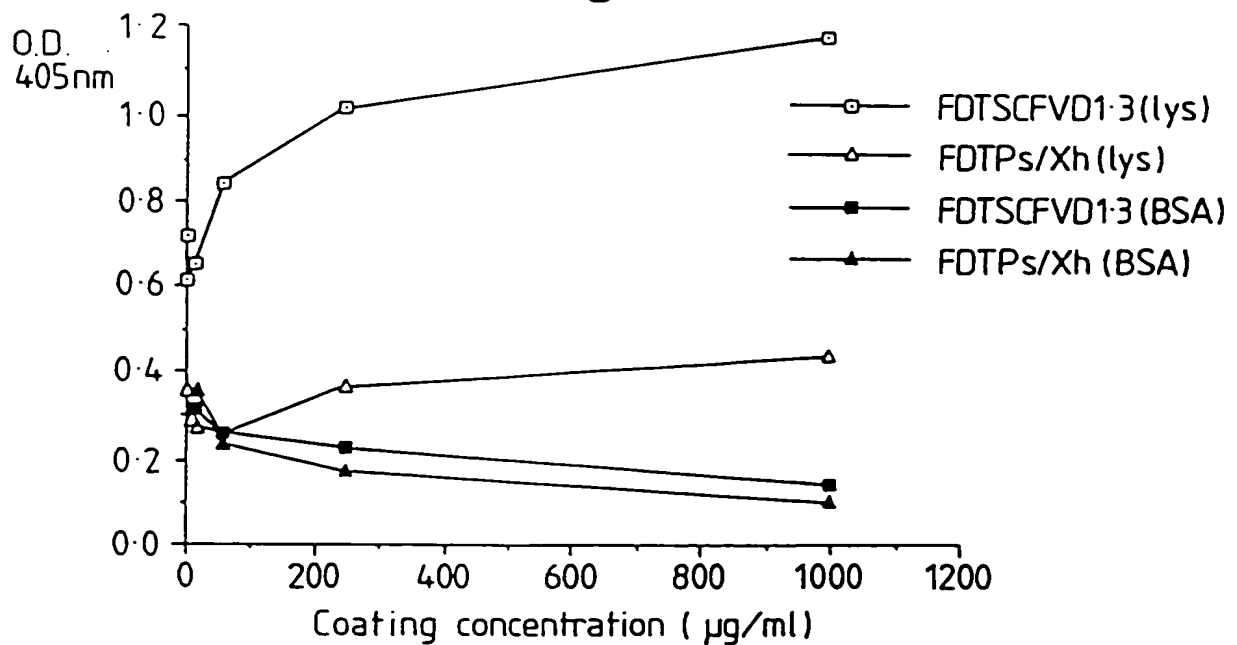


Fig.7.



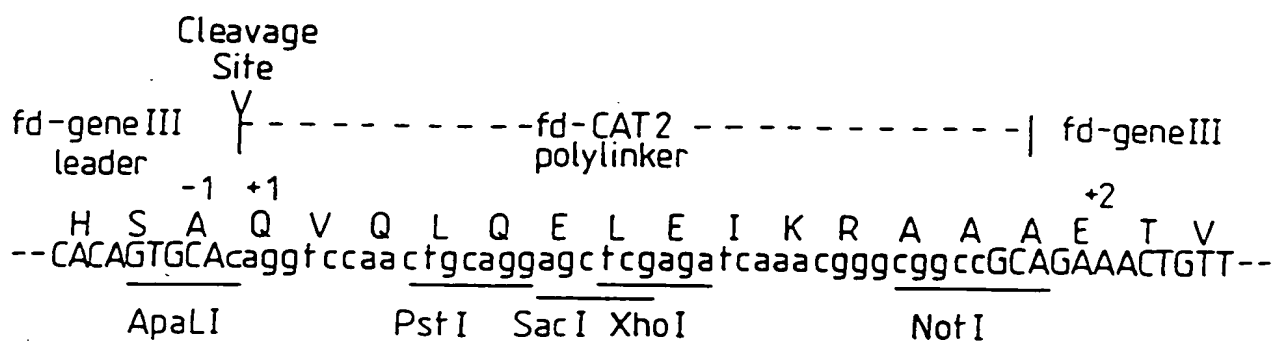
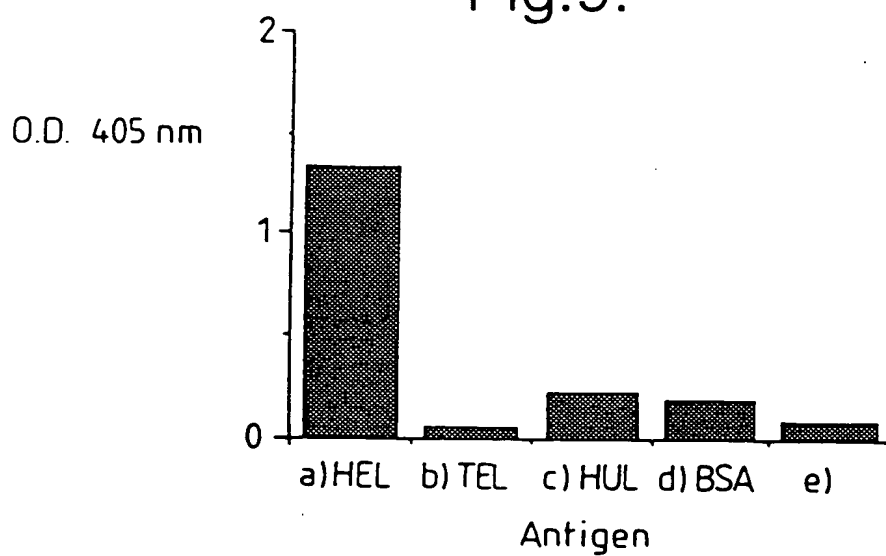


Fig.9.



Year	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100
1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	

M K Y L L P T A A
GCATGCAAATTCTATTTCAAGGAGACAGTCATAATGAAATACCTATTGGCTACGGCAGCC
10 20 30 40 50 60
A G L L L L A A Q P A M A Q V Q L Q E S
GCTGGATTGTTATTACTGCTGCCCAACCAGCGATGGCCCAGGTGCAGCTGCAGGAGTCA
70 80 90 100 110 120
G P G L V A P S Q S L S I T C T V S G F
GGACCTGGCCTGGTGGCGCCCTCACAGAGCCTGTCCATCACATGCACCGTCTCAGGGTTC
130 140 150 160 170 180
S L T G Y G V N W V R Q P P G K G L E W
TCATTAAACCGGCTATGGTGTAAACTGGGTTCGCCAGCCTCCAGGAAAGGGTCTCGAGTGG
190 200 210 220 230 240
L G M I W G D G N T D Y N S A L K S R L
CTGGGAATGATTTGGGGTGATGGAAACACAGACTATAATTACAGCTCTCAAATCCAGACTG
250 260 270 280 290 300
S I S K D N S K S Q V F L K M N S L H T
AGCATCAGCAAGGACAACTCCAAGAGCCAAGTTTTCTTAAAAATGAACAGTCTGCACACT
310 320 330 340 350 360
D D T A R Y Y C A R E R D Y R L D Y W G
GATGACACAGCCAGGTACTACTGTGCCAGAGAGAGAGATTATAGGCTTGACTACTGGGGC
370 380 390 400 410 420
Q G T T V T V S S A S T K G P S V F P L
CAAGGCACCAAGGTACCGTCTCCTCAGCCTCCACCAAGGGCCCATCGGTCTTCCCCCTG
430 440 450 460 470 480
A P S S K S T S G G T A A L G C L V K D
GCACCCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCTGGTCAAGGAC
490 500 510 520 530 540

[illegible]

N Y L A W Y Q Q K Q G K S P Q L L V Y Y
ACAATTATTTAGCATGGTATCAGCAGAAACAGGGAAATCTCTCTCAGCTCCTGGTCTATT
970 980 990 1000 1010 1020

[illegible]

R G E S * *
ACCGGGGAGAGTCATAGTAAGAATTC
1510 1520

Fig.10 (Cont 3).

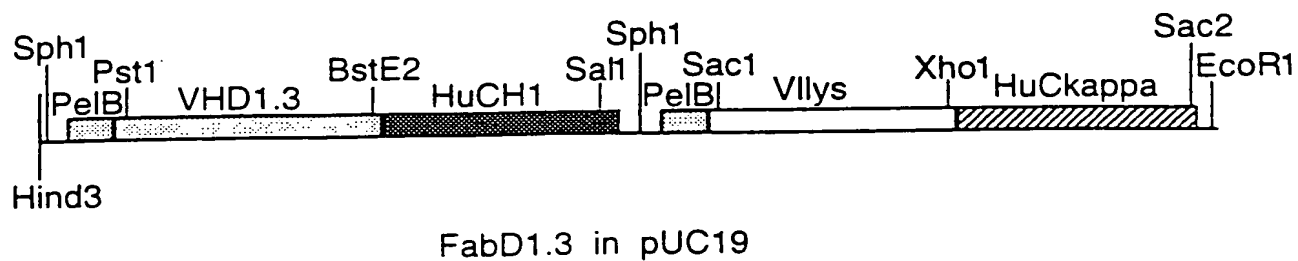
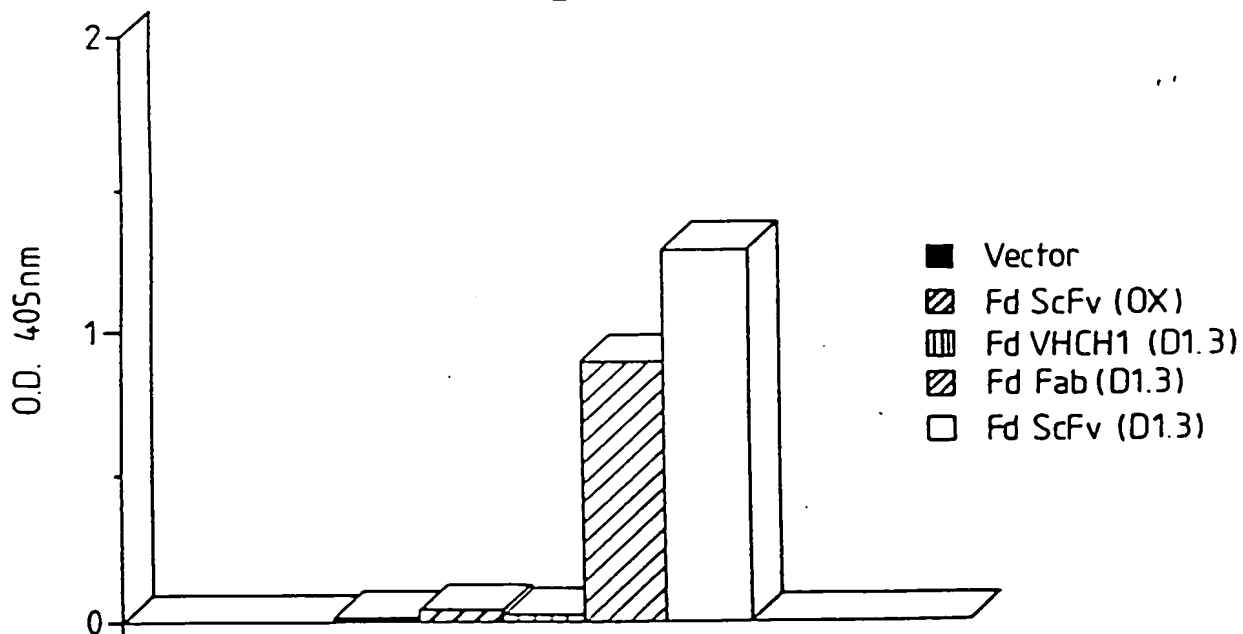



Fig.11.





date	place	temperature	direction	speed	state	remarks
11/11/1911	San Francisco	61°	SE	10	11	11
11/12/1911	San Francisco	61°	SE	10	11	11
11/13/1911	San Francisco	61°	SE	10	11	11
11/14/1911	San Francisco	61°	SE	10	11	11
11/15/1911	San Francisco	61°	SE	10	11	11
11/16/1911	San Francisco	61°	SE	10	11	11
11/17/1911	San Francisco	61°	SE	10	11	11
11/18/1911	San Francisco	61°	SE	10	11	11
11/19/1911	San Francisco	61°	SE	10	11	11
11/20/1911	San Francisco	61°	SE	10	11	11
11/21/1911	San Francisco	61°	SE	10	11	11
11/22/1911	San Francisco	61°	SE	10	11	11
11/23/1911	San Francisco	61°	SE	10	11	11
11/24/1911	San Francisco	61°	SE	10	11	11
11/25/1911	San Francisco	61°	SE	10	11	11
11/26/1911	San Francisco	61°	SE	10	11	11
11/27/1911	San Francisco	61°	SE	10	11	11
11/28/1911	San Francisco	61°	SE	10	11	11
11/29/1911	San Francisco	61°	SE	10	11	11
11/30/1911	San Francisco	61°	SE	10	11	11

[illegible]

Q V Q L Q E S G G G L V Q P G G
CAG GTG CAG CTG CAG GAG TCA GGA GGA GGC TTG GTA CAG CCT GGG GGT
PstI
S L R L S C A T S G F T F S N Y
TCT CTG AGA CTC TCC TGT GCA ACT TCT GGG TTC ACC TTC AGT AAT TAC
Y M G W V R Q P P G K A L E W L
TAC ATG GGC TGG GTC CGC CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG
G S V R N K V N G Y T T E Y S A
GGT TCT GTT AGA AAC AAA GTT AAT GGT TAC ACA ACA GAG TAC AGT GCA
S V K G R F T I S R D N F Q S I
TCT GTG AAG GGG CGG TTC ACC ATC TCC AGA GAT AAT TTC CAA AGC ATC
L Y L Q I N T L R T E D S A T Y
CTC TAT CTT CAA ATA AAC ACC CTG AGA ACT GAG GAC AGT GCC ACT TAT
Y C A R G Y D Y G A W F A Y W G
TAC TGT GCA AGA GGC TAT GAT TAC GGG GCC TGG TTT GCT TAC TGG GGC
Q G T L V T v s s g g g g s g g g g s
CAA GGG ACC CTG GTC ACC gtc tcc tca ggtagggcggttcaggcggagggtggcct
BstEII
g g g g s d i E L T Q T P L S L P V
ggcggtaggcggatcgagac atc GAG CTC ACC CAA ACT CCA CTC TCC CTG CCT GTC
SacI
S L G D Q A S I S C R S S Q S I
AGT CTT GGA GAT CAA GCC TCC ATC TCT TGC AGA TCT AGT CAG AGC ATT
V H S N G N T Y L E W Y L Q K P
GTA CAT AGT AAT GGA AAC ACC TAT TTA GAA TGG TAC CTG CAG AAA CCA
PstI
G Q S P K L L I Y K V S N R F S
GGC CAG TCT CCA AAG CTC CTG ATC TAC AAA GTT TCC AAC CGA TTT TCT
G V P D R F S G S G S G T D F T
GGG GTC CCA GAC AGG TTC AGT GGC AGT GGA TCG GGG ACA GAT TTC ACA
L K I S R V E A E D L G V Y Y C
CTC AAG ATC AGC AGA GTG GAG GCT GAG GAT CTG GGA GTT TAT TAC TGC
F Q G S H V P Y T F G G G T K L
TTT CAA GGT TCA CAT GTT CCG TAC ACG TTC GGA GGG GGG ACC AAG CTC
E I K R
GAG ATC AAA CGG
XhoI

Fig.14.

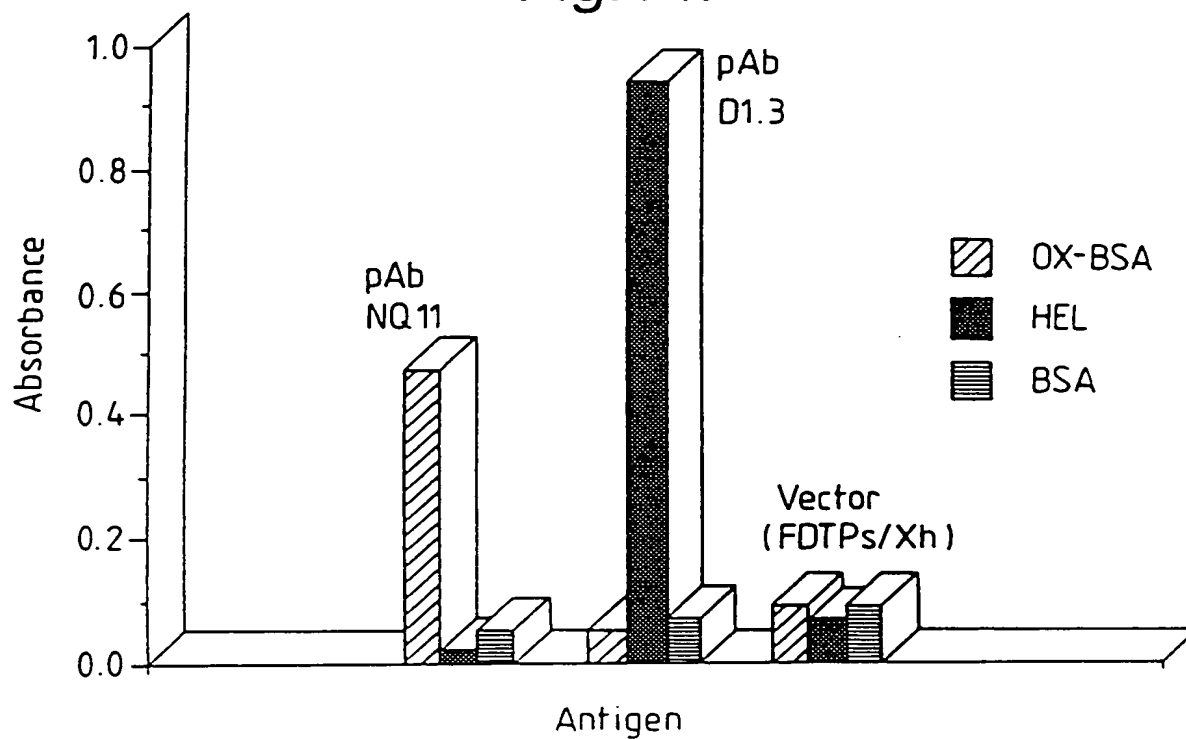


Fig.15.

5' END

TCT CAC AGT GCA CAA ACT GTT GAA CGG ACA CCA GAA ATG CCT GTT CTG
 ApaL1

3' END

K A A L G L K
 AAA GCC GCT CTG GGG CTG AAA GCG GCC GCA GAA ACT GTT GAA AGT etc.
 Not I

Fig.16 (i).

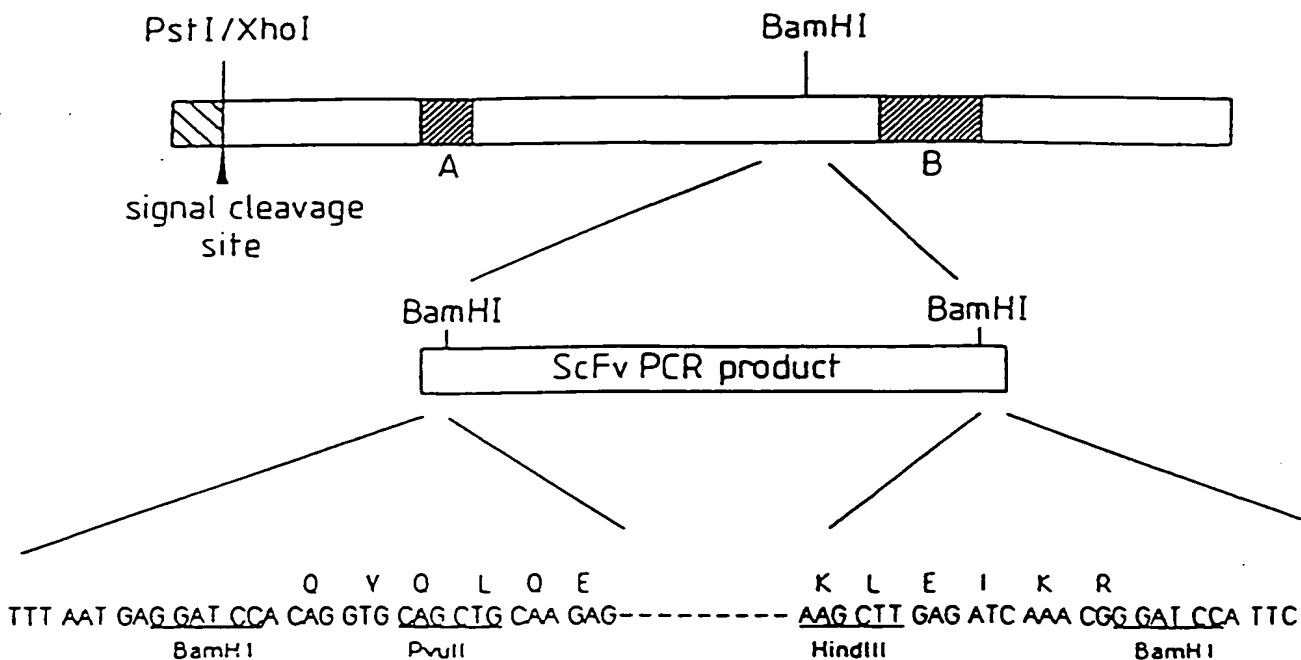


Fig.16 (ii).

A (1834) 5' GAG GGT GGT GGC TCT
 " " "C " "
 " " "C " "
 " " "C " ACT 3'(1839)

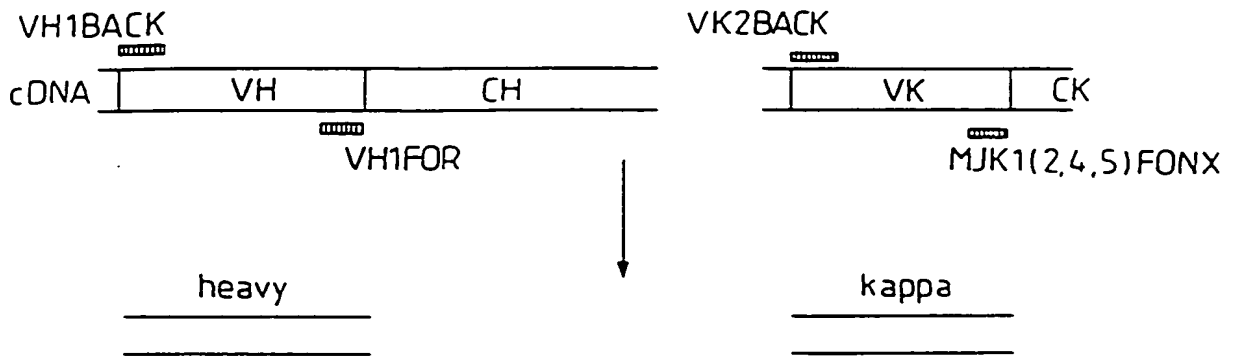
B (2284) 5' - GGC GGC GGC TCT
 - GGT GGT GGT -
 - " GGC GGC -
 GAG - " GGC -
 " - " GGT -
 - - " GGC -
 - - " GGT -
 - " " GGC - 3'(2379)

Reverse complement of mutagenic
 oligo G38amlink

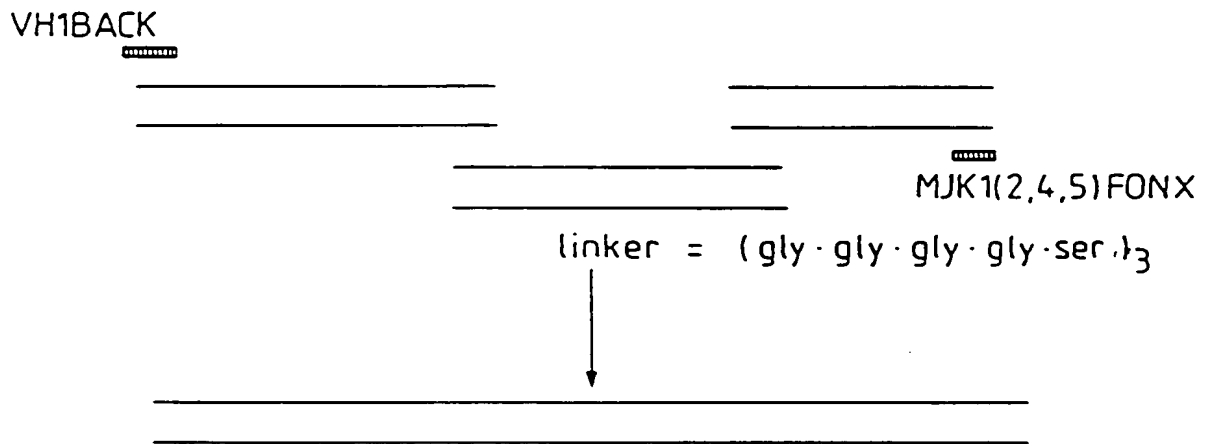
5' GAG GGT GGC GGA TCC
 T
 GAG GGT GGC GG 3'

Fig.17.

1) PRIMARY PCR



2) ASSEMBLY PCR



3) ADDING RESTRICTION SITES

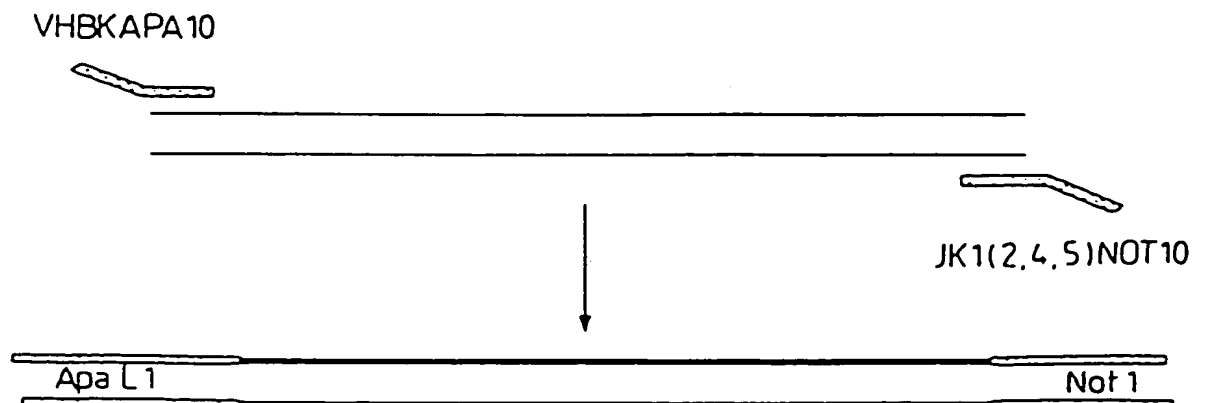
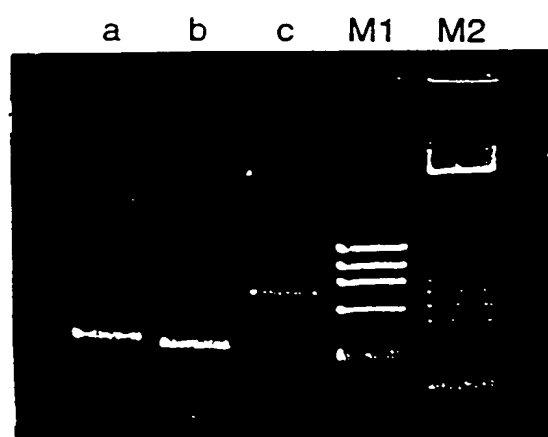


Fig.18.



666707 6/2/88

Fig.19.

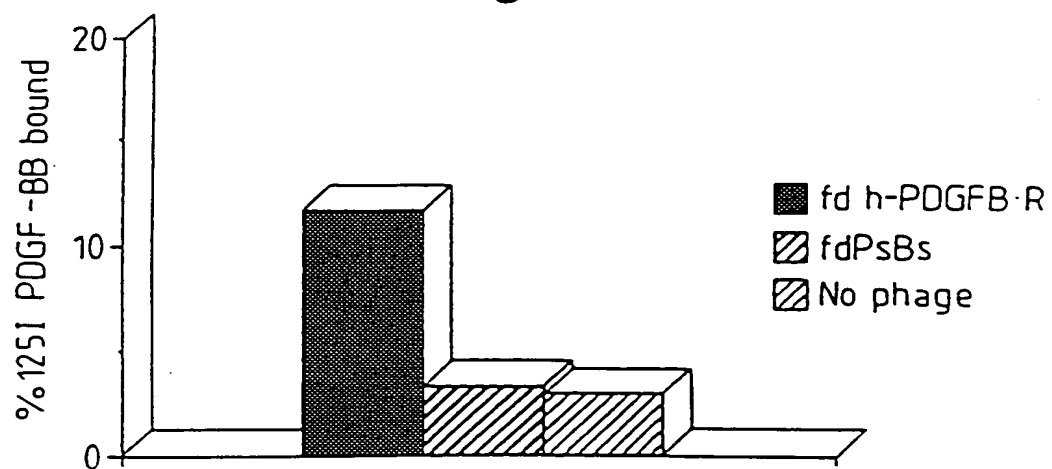


Fig.20.

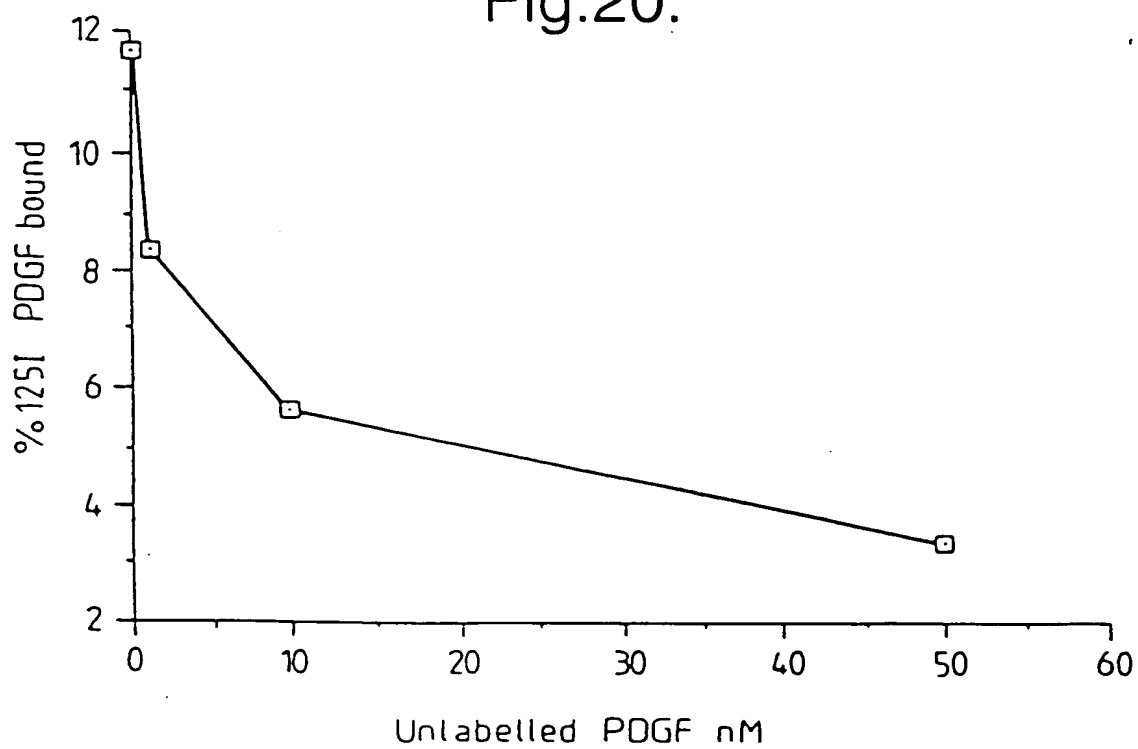


Fig.21.

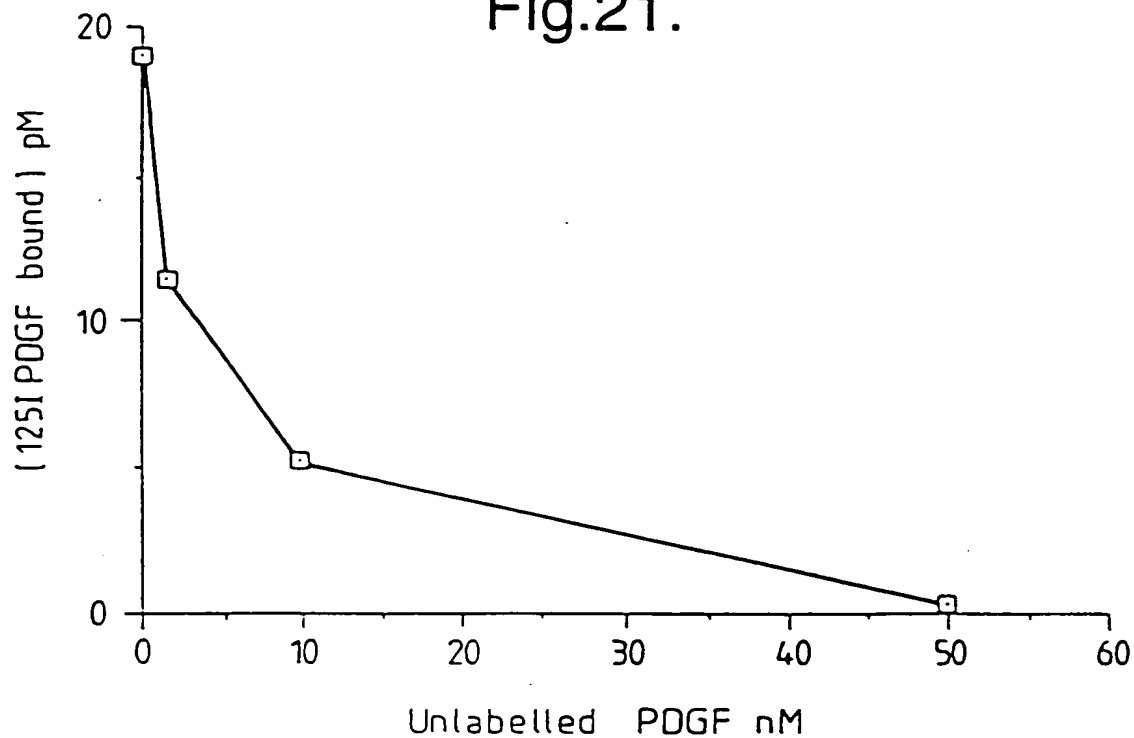


Fig.22.

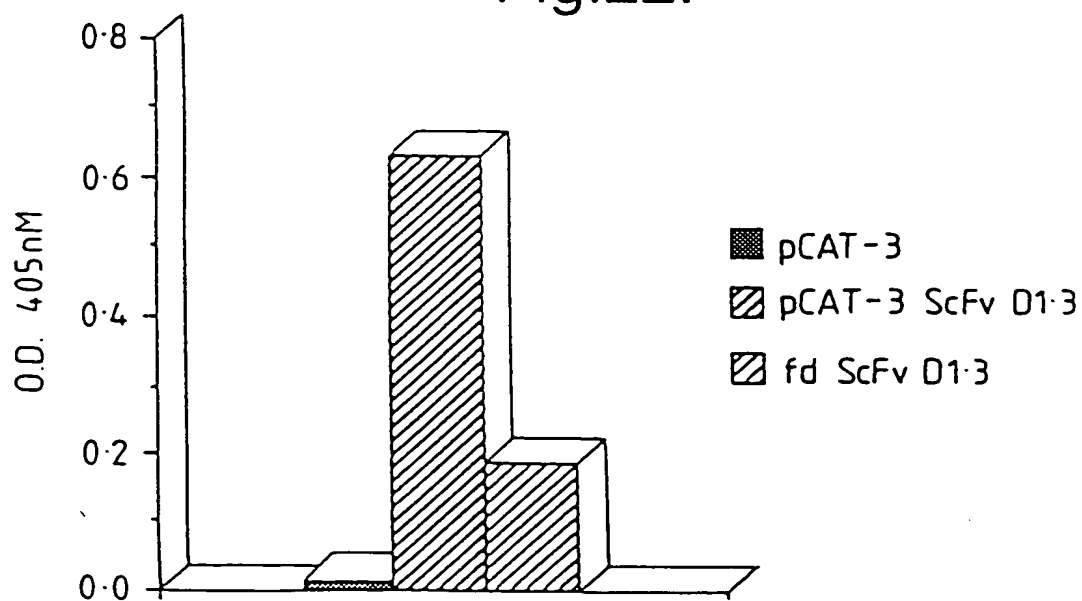


Fig.23(i)

d
M

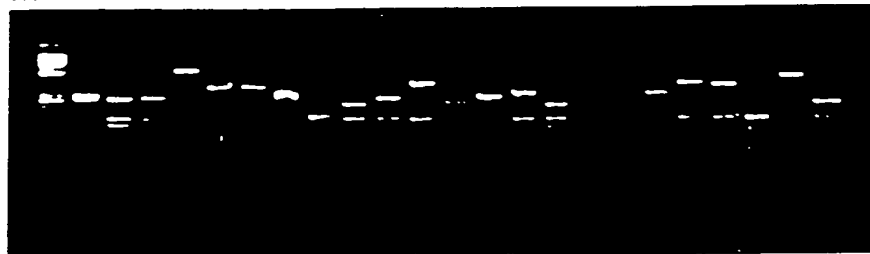
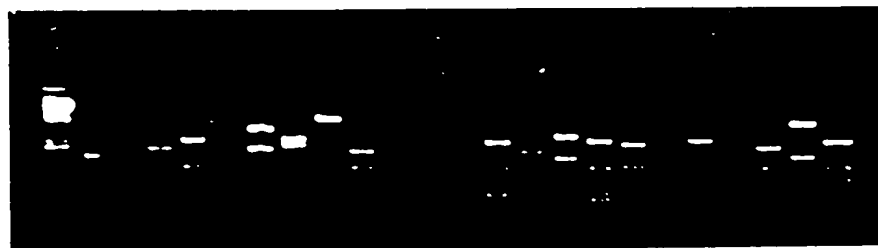


Fig.23(ii)

M



66701 66702 66703 66704 66705 66706 66707 66708 66709 66710 66711 66712 66713 66714 66715 66716 66717 66718 66719 66720 66721 66722 66723 66724 66725 66726 66727 66728 66729 66730 66731 66732 66733 66734 66735 66736 66737 66738 66739 66740 66741 66742 66743 66744 66745 66746 66747 66748 66749 66750 66751 66752 66753 66754 66755 66756 66757 66758 66759 66760 66761 66762 66763 66764 66765 66766 66767 66768 66769 66770 66771 66772 66773 66774 66775 66776 66777 66778 66779 66780 66781 66782 66783 66784 66785 66786 66787 66788 66789 66790 66791 66792 66793 66794 66795 66796 66797 66798 66799 66800

VH sequences

from combinatorial library:

	CDR1	CDR2	CDR3	
A	QVQLQSGGPELAPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS x4 1
B	QVQLQSGGPELAKPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS x9 1
C	QVQLQSGGPELVKPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS x3 1
D	QVQLQSGGPELVKPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS x3 1
E	QVQLQSGGPELVKPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS x3 1
F	QVQLQSGGPELVKPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS x3 1
G	QVQLQSGGPELVKPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS x3 1
H	QVQLQSGGPELVKPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS x3 1

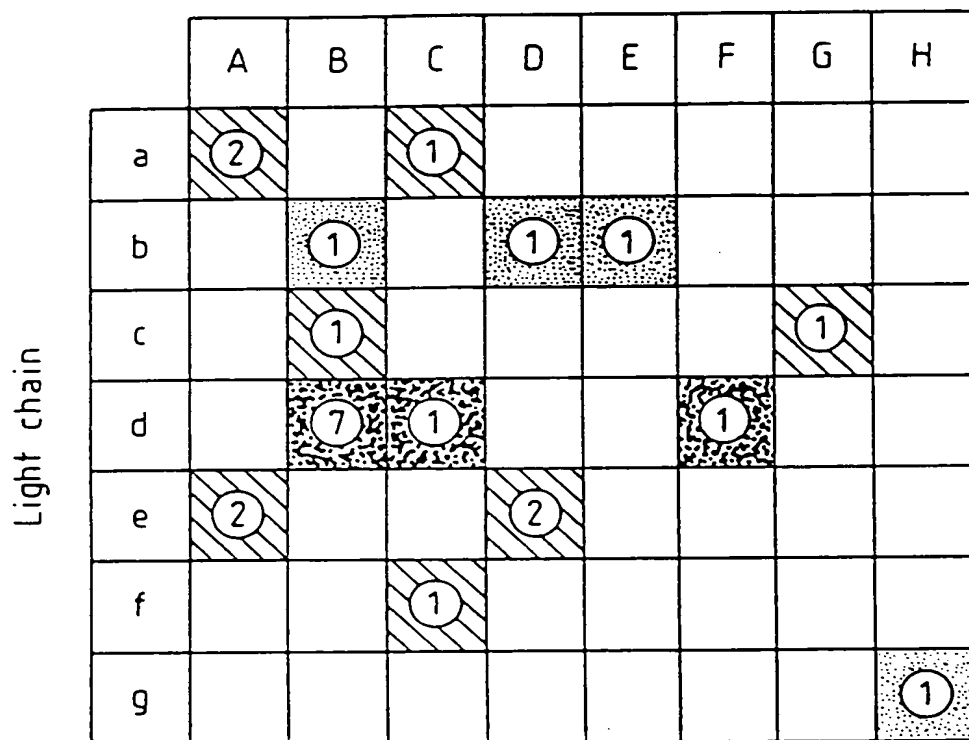
Ir m hierarchical library VH-rep x Vc-d:

I	QVQLQSGGPELAPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS 1
J	QVQLQSGGPELAPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS 1
K	QVQLQSGGPELAPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS x3 1
L	QVQLQSGGPELAPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS x2 1
M	QVQLQSGGPELAPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS 1
N	QVQLQSGGPELAPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS 1
O	QVQLQSGGPELAPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS 1
P	QVQLQSGGPELAPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS 1
Q	QVQLQSGGPELAPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS 1
R	QVQLQSGGPELAPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS 1
S	QVQLQSGGPELAPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS x2 1
T	QVQLQSGGPELAPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS x6 1
U	QVQLQSGGPELAPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS 1
V	QVQLQSGGPELAPGASVKMSCKASGTTT	YINPSSGYTETYNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVYYCAR	WQGGTTTVSS 1

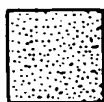
Fig.24.

Fig.25.

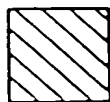
HEAVY CHAIN



OD_{405nm} in ELISA



0.2-0.9



0.9-2.0



>2.0

09417479-101309

Fig.26(a).

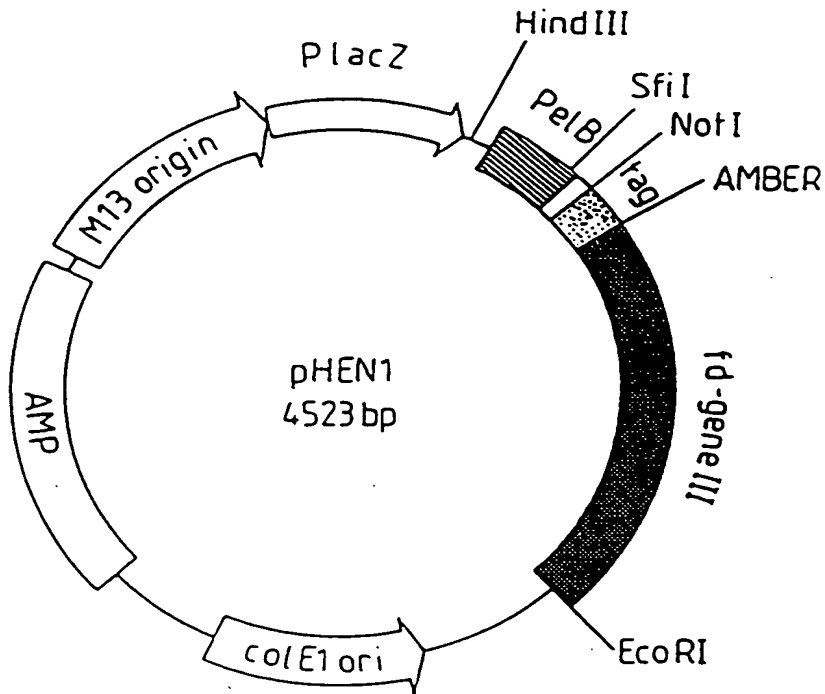


Fig.26(b).

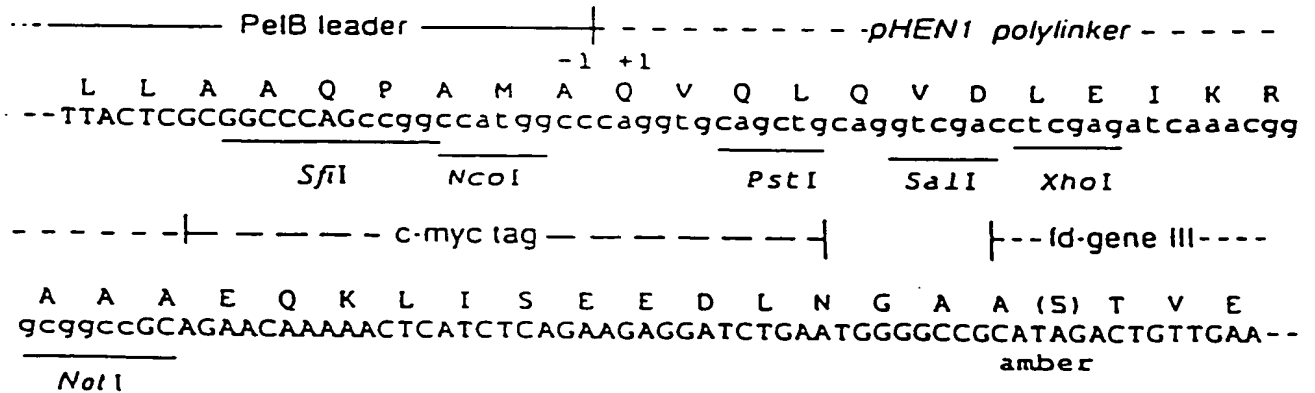


Fig.27.

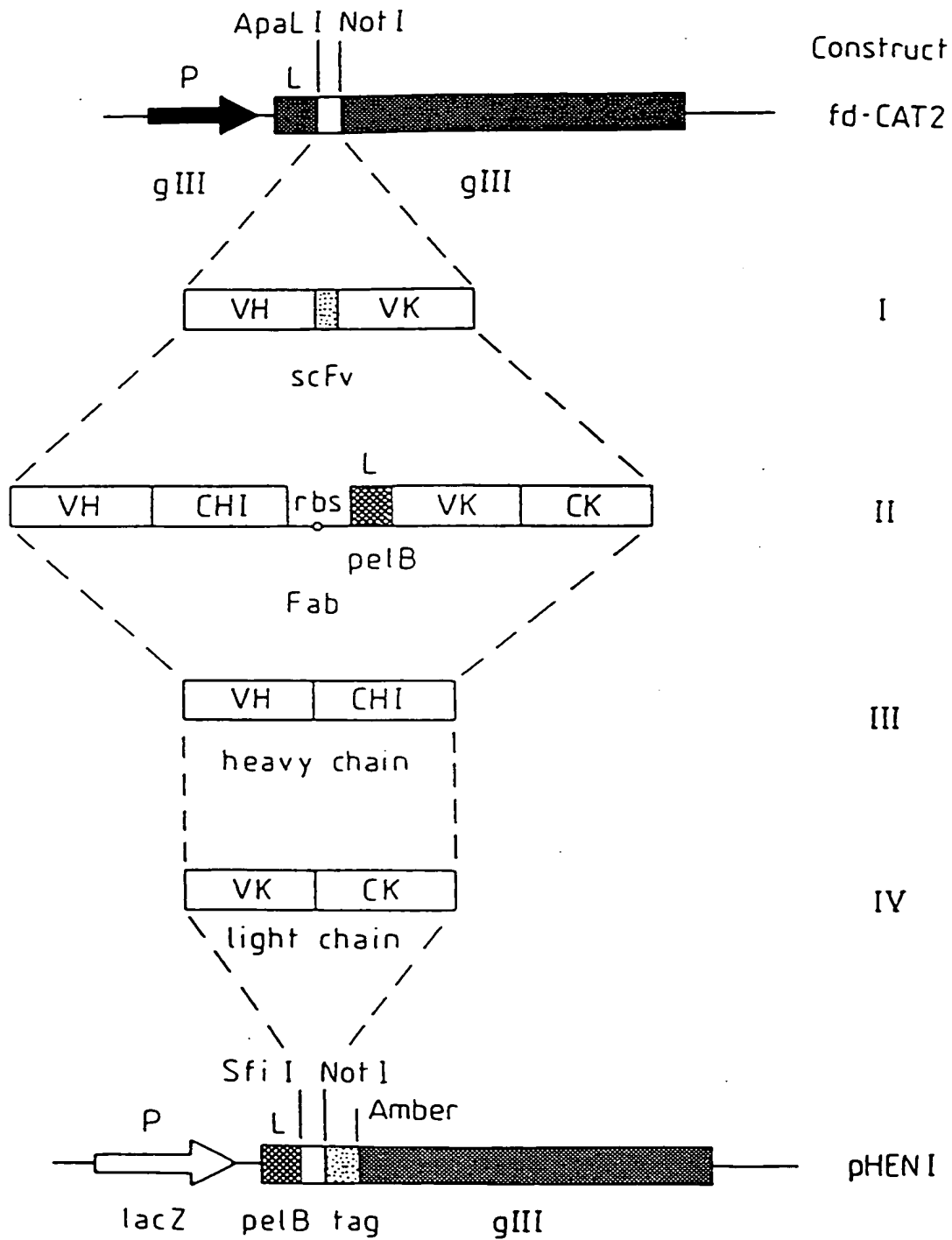


Fig.28.

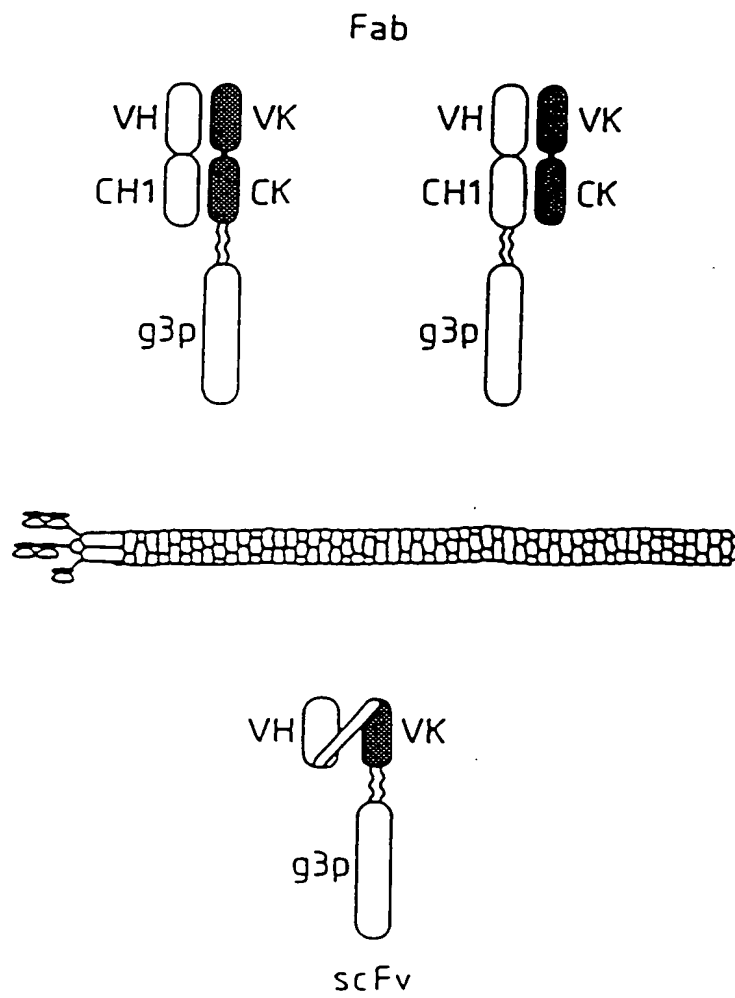


Fig.29.

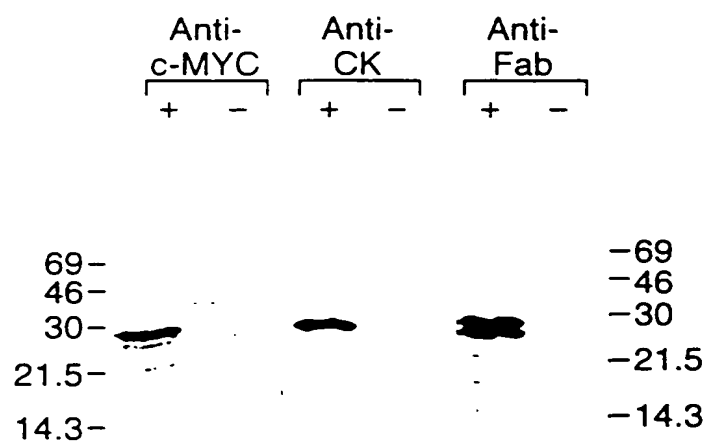


Fig.30.

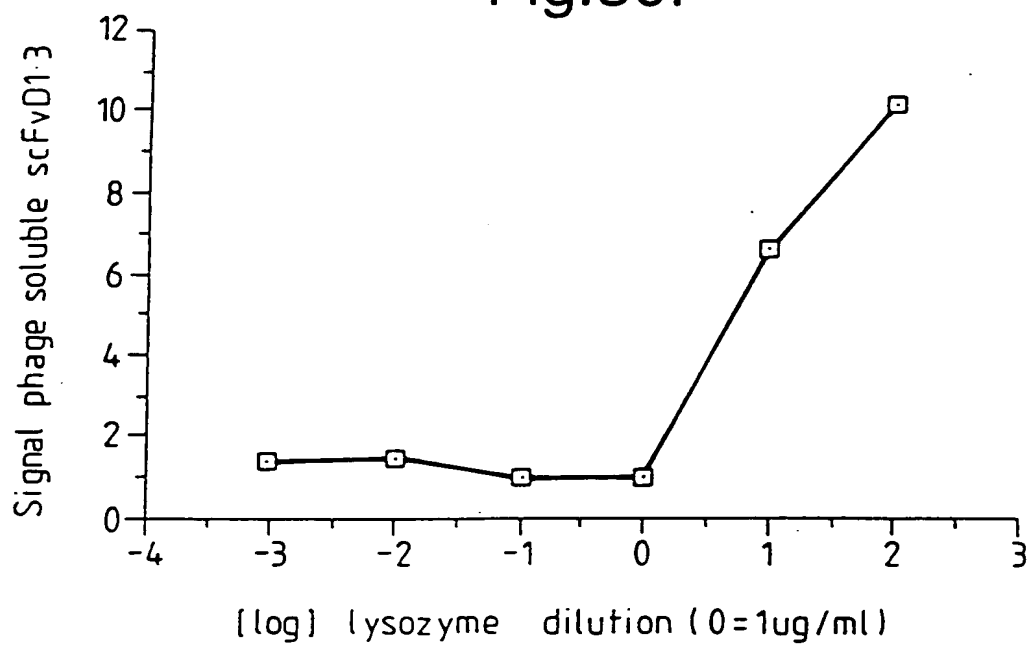


Fig.31.

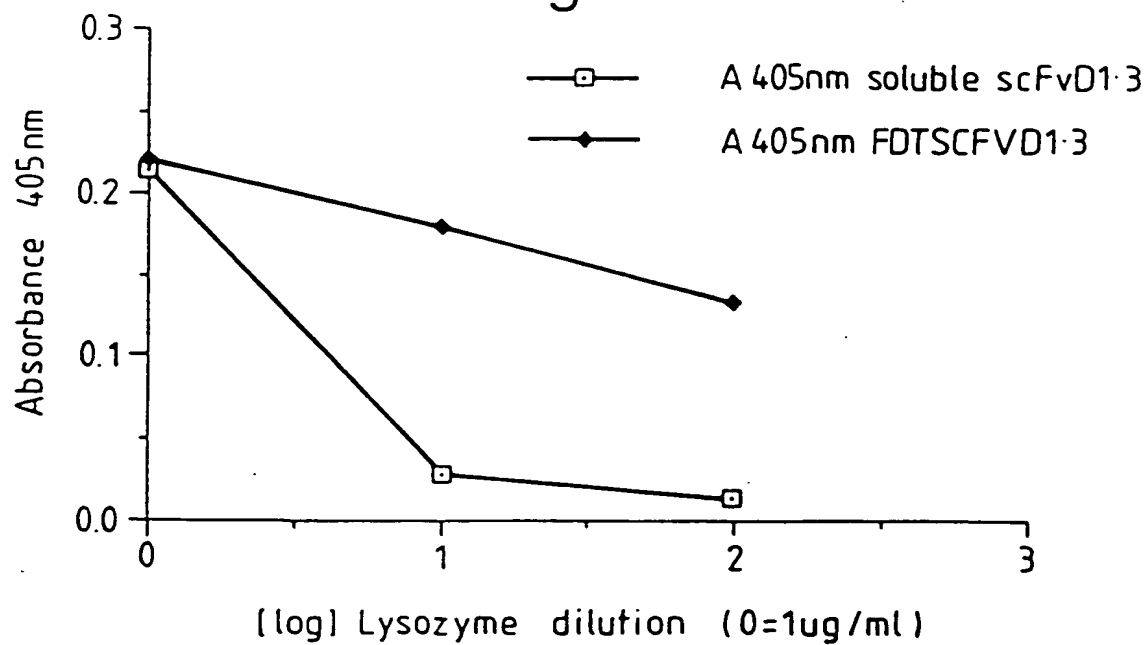


Fig.32.

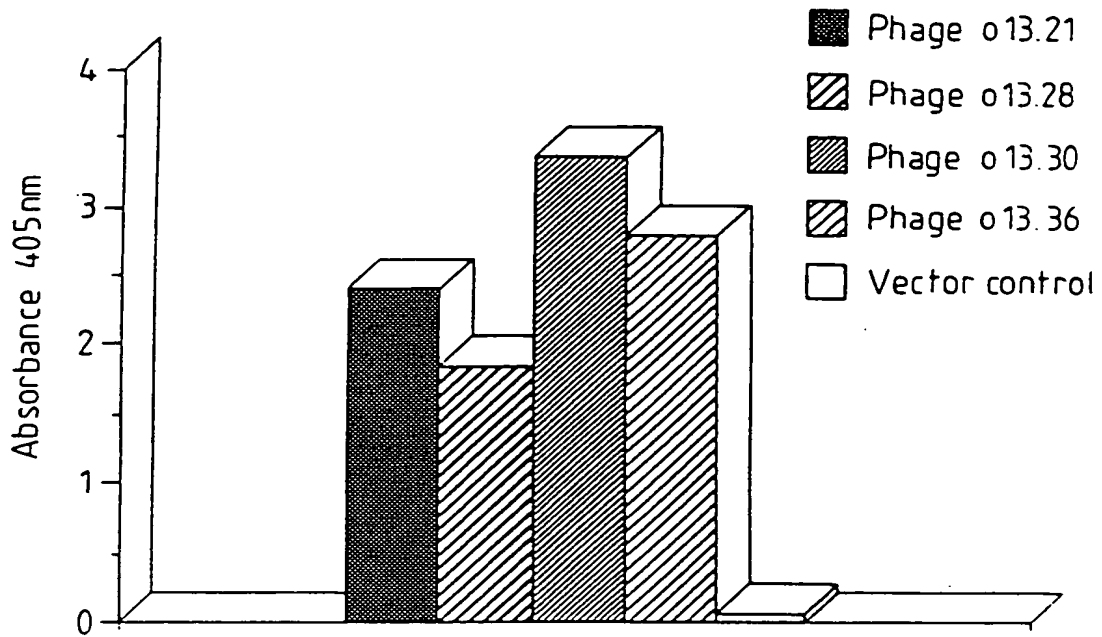


Fig.33.

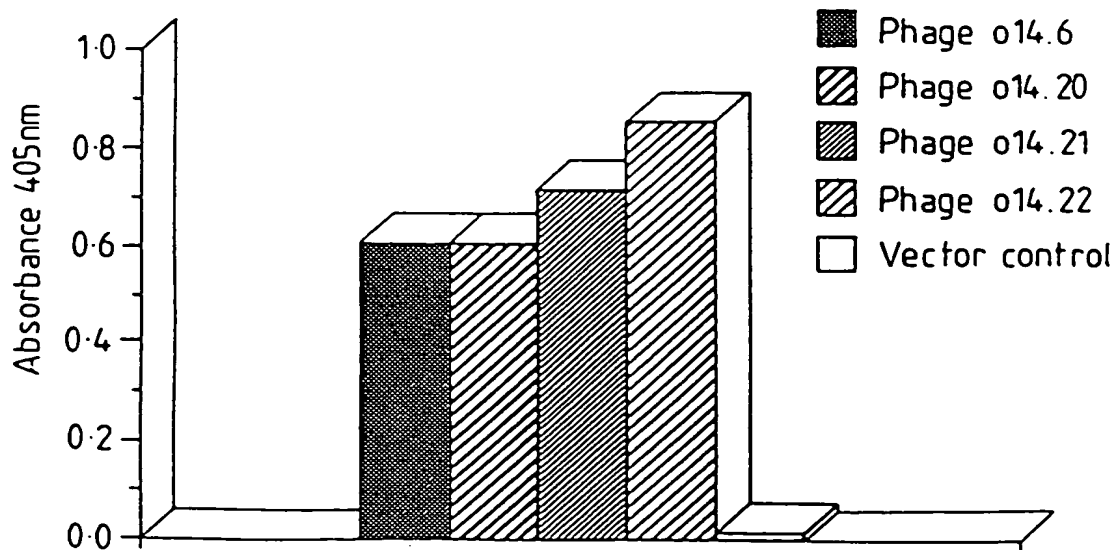


Fig.34.

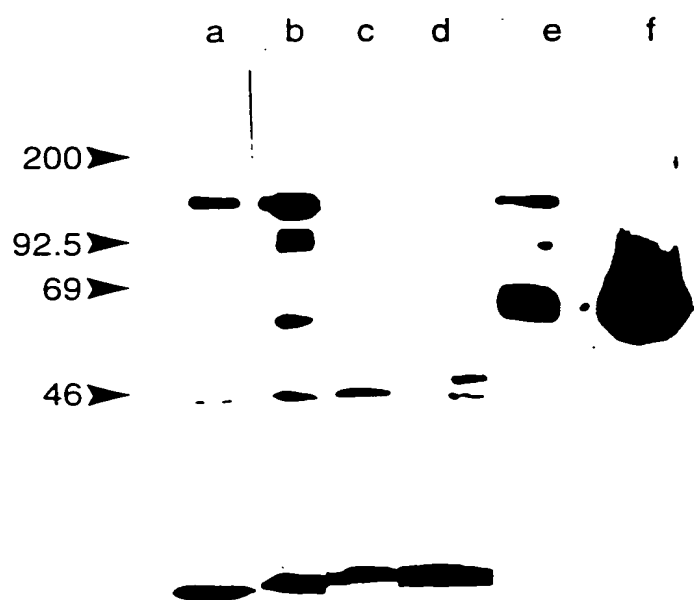


Fig.35A.

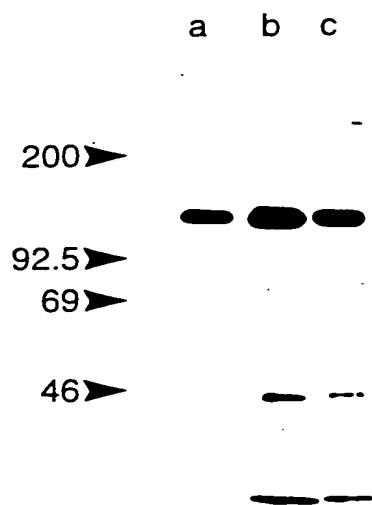


Fig.35B.

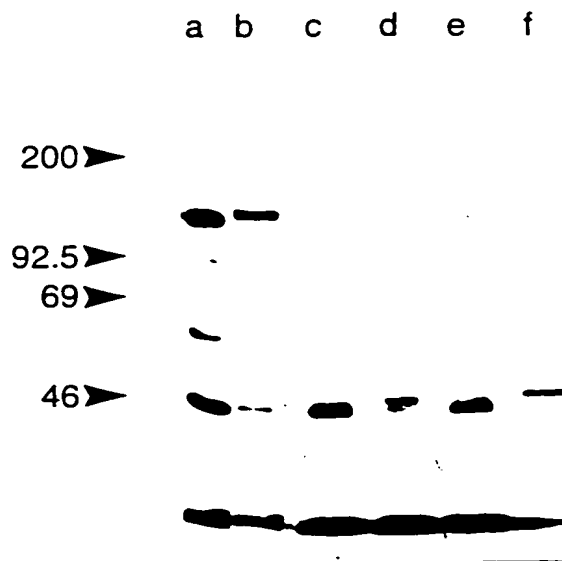


Fig.36.

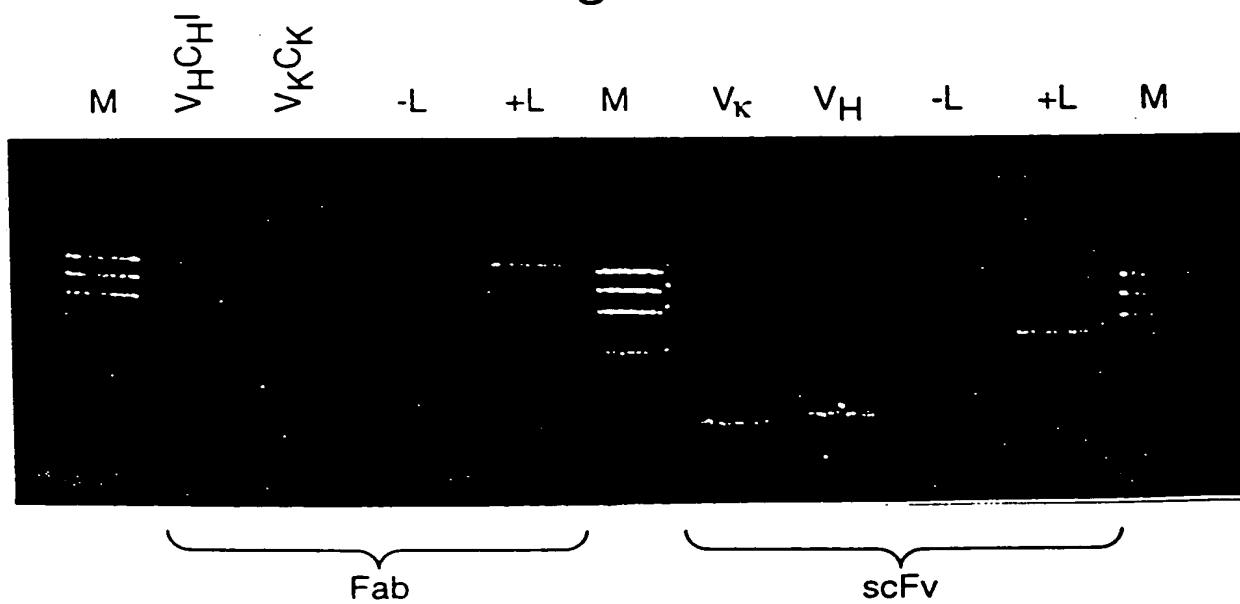
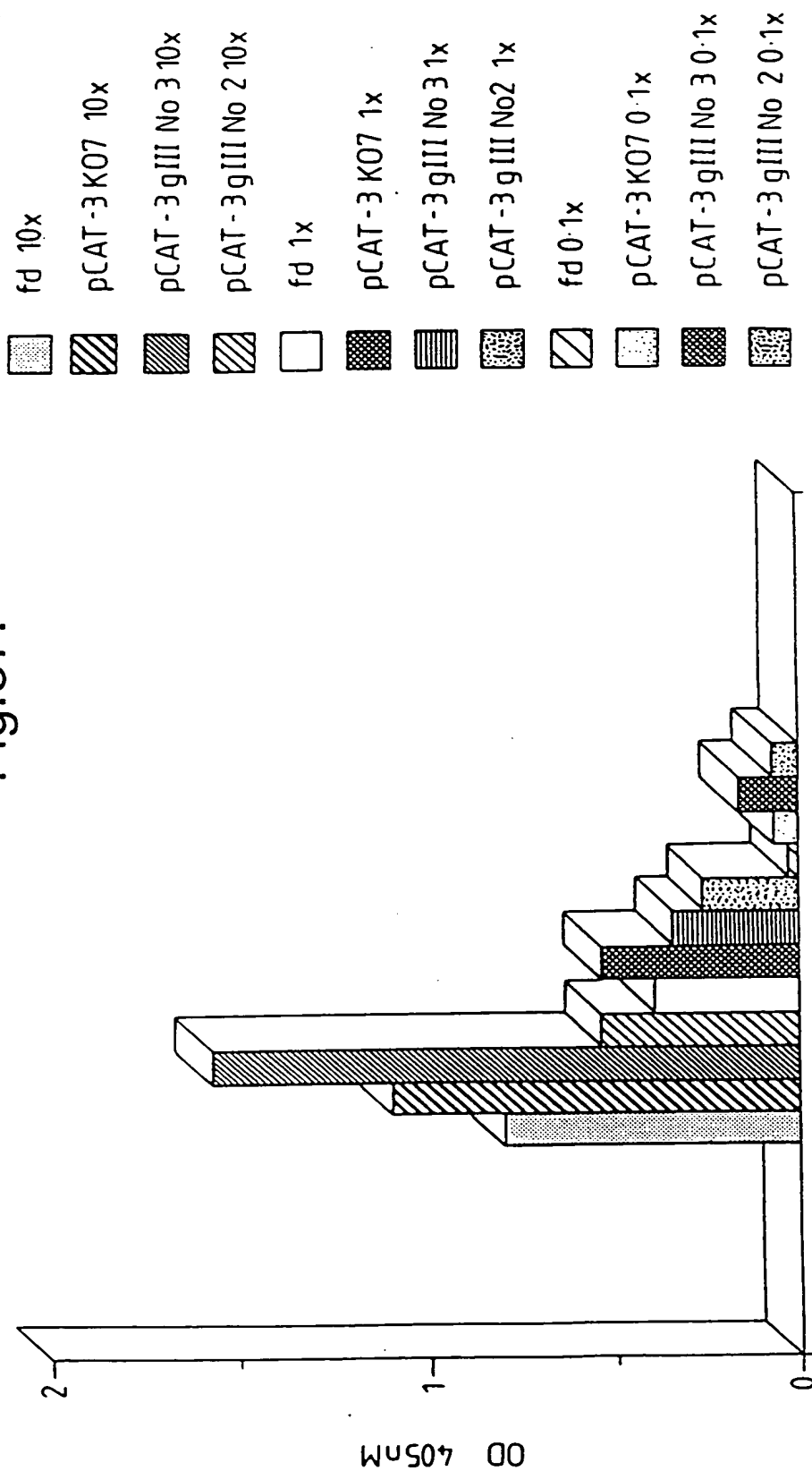


Fig.37.



bioRxiv preprint doi: <https://doi.org/10.1101/201909.101399>; this version posted September 10, 2019. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Fig.38A.



Fig.38B.

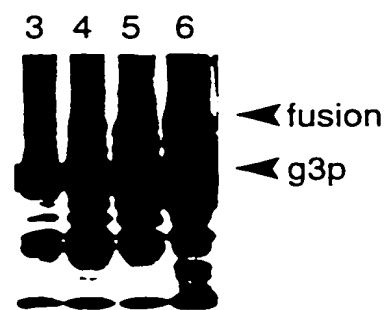


Fig.39.

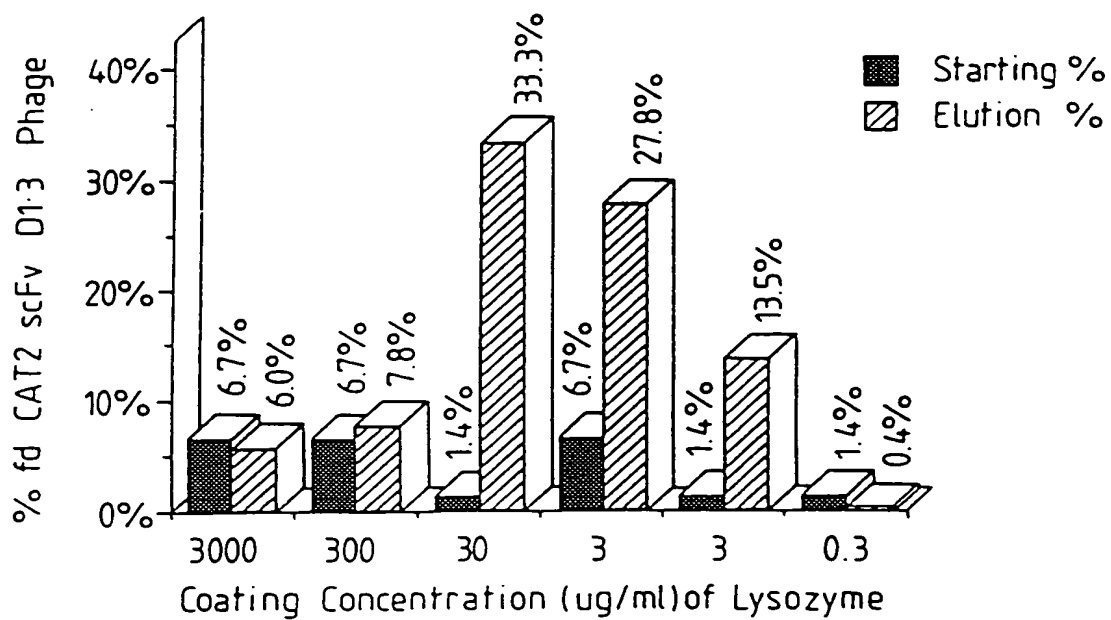


Fig.40.

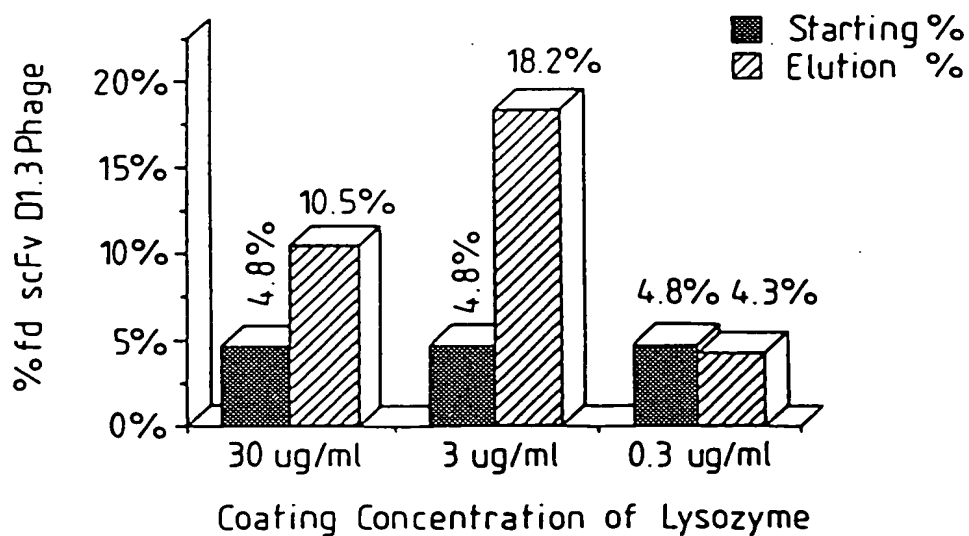


Fig.41.

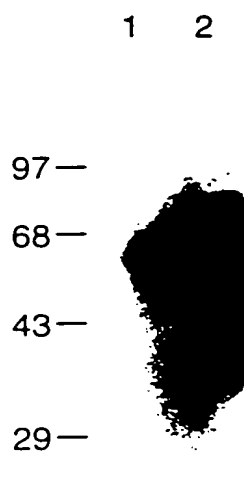


Fig.42.

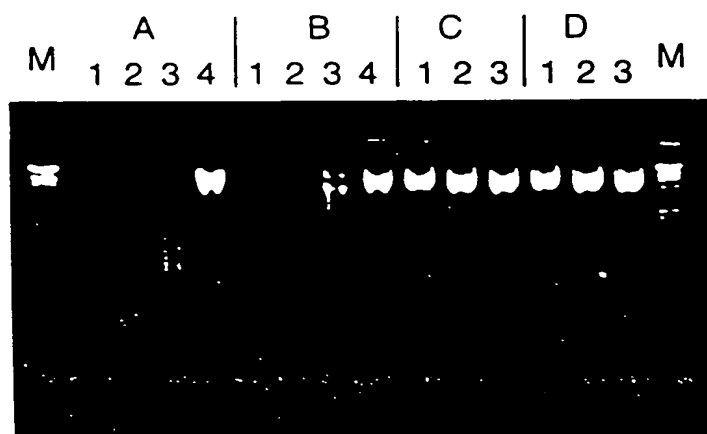


Fig.43.

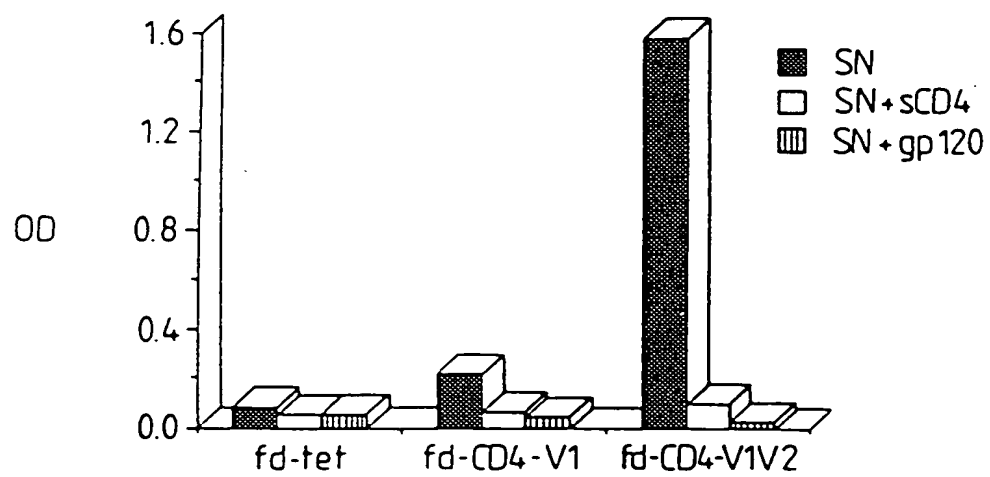


Fig.44 (i).

10	20	30	40	50	60	70	80	90
TTCTATTCTCACAGTGCACAGGTCCAGCTGCAGCAGTCTGGGGCTGAGCTTGTGAAGCCTGGGGCTTCAGTGAAGCTGTCTCCTGCAAGGCT								
AAGATAAGAGTGTACGTTGCCAGGTCCAGCTGCAGACCCCGACTCGAACACTTCGGACCCCGAAGTCACCTTCGACAGACGTTCCGA								
PheTyrSerHisSerAlaGlnValGlnLeuGlnSerGlyAlaGluLeuValLysProGlyAlaSerValLysLeuSerCysLysAla								
100	110	120	130	140	150	160	170	180
TCTGGCTACACCTTACCCAGCTACTGGATGCACCTGGGTGAAGCAGAGGCCCTGGACGAGGCCCTTGAGTGGATTGGAAGGATTGATCCTAAT								
AGACCCGATGTGGAAGTGGTCGATGACCTACGTGACCCACTTCGTCTCCGGACCTGCTCCGGAACCTCACCTAACCTTCTCTAACTAGGATTA								
SerGlyTyrThrPheThrSerTyrTrpMetHisTrpValLysGlnArgProGlyArgGlyLeuGluTrpIleGlyArgIleAspProAsn								
190	200	210	220	230	240	250	260	270
AGTGGTGGTACTAAGTACAATGAGAAGTTCAAGAGCAAGGCCACACTGACTGTAGACAAACCCCTCCAGCACAGCCCTACATGCAGCTCAGC								
TCACCAACCATGATTCTACTCTTCAAGTTCTCGTTCGGGTGTGACTGACATCTGTTTGGGAGGTCGTGTCGGATGTACGTCGAGTCG								
SerGlyGlyThrLysTyrAsnGluLysPheLysSerLysAlaThrLeuThrValAspLysProSerSerThrAlaTyrMetGlnLeuSer								
280	290	300	310	320	330	340	350	360
AGCCTGACATCTGAGGACTCTGCGGTCTATTATTGTGCAAGNTACGACTACGGTAGTAGCTACTACTTTGACTACTGGGGCCAAAGGGACC								
TCGGACTGTAGACTCCTGAGACGCCAGATAATAACACGTTCTATGCTGATGCCATCATCGATGATGAACACTGATGACCCCGGTTCCCTGG								
SerLeuThrSerGluAspSerAlaValTyrTyrCysAlaArgTyrAspTyrGlySerSerTyrTyrPheAspTyrTrpGlyGlnGlyThr								
370	380	390	400	410	420	430	440	450
ACGGTCAACCGTCTCCTCAGGTGAGGCGGTTTCAGGCGGAGGTGGCTCTGGCGGTGGCGGATCCAGGCTGTTGGGACACAGGAATCTGCA								
TGCCAGTGGCAGAGGATCCACCTCCGCCAAGTCCGCCCTCCACCGAGACCGCCACCGCTAGGTCGACAAACCCCTGTGTCCTTAGACGT								
ThrValThrValSerSerGlyGlyGlySerGlyGlyGlySerGlyGlyGlySerGlnAlaValGlyThrGlnGluSerAla								
460	470	480	490	500	510	520	530	540
CTCACACATCACCTGGTGAAACAGTCACACTCACTTGTGCGCTCAAGTACTGGGGCTGTTACAACACTAGTAACATATGCCAAGTGGGTCCAA								
GAGTGGTGTAGTGACCACTTTGTGTCAGTGTGAGTGAACAGCGAGTTTCATGACCCCGACAAATGTTGATCATATTGATACGGTTGACCCAGGTT								
LeuThrThrSerProGlyGluThrValThrLeuThrCysArgSerSerThrGlyAlaValThrThrSerAsnTyrAlaAsnTrpValGln								
550	560	570	580	590	600	610	620	630
GAAAAACCAAGATCATTTATTCACTGGTCTAATAGGTGTACCAACACCGAGCTCCAGGTGTTCTTCCAGGATTTCTCAGGCTCCCTGATT								
CTTTTGGTCTAGTAAATAAGTGACCAAGATTATCCACCATGGTTGTTGGCTCGAGGTCCACAAAGGACGGTCTAAGAGTCCGAGGGACTAA								
GluLysProAspHisLeuPheThrGlyLeuIleGlyGlyThrAsnAsnArgAlaProGlyValProAlaArgPheSerGlySerLeuIle								

Fig. 44 (ii).

Fig.45.

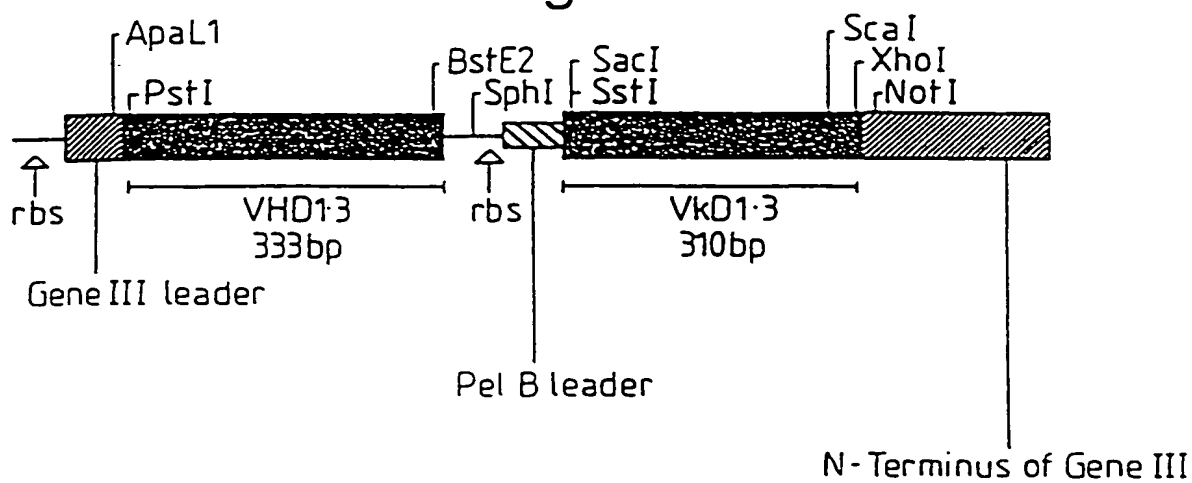


Fig.46.

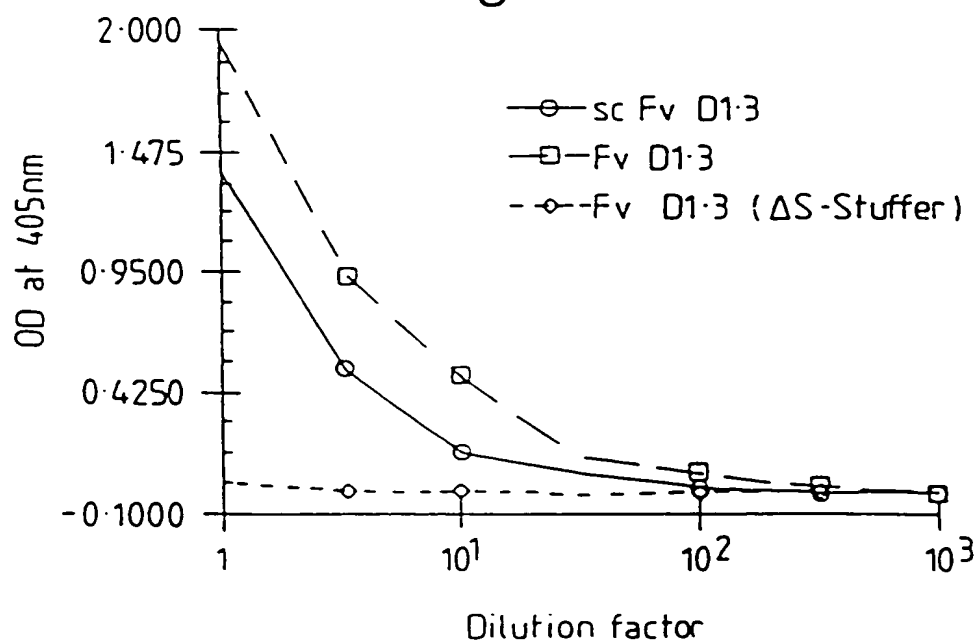


Fig.47.

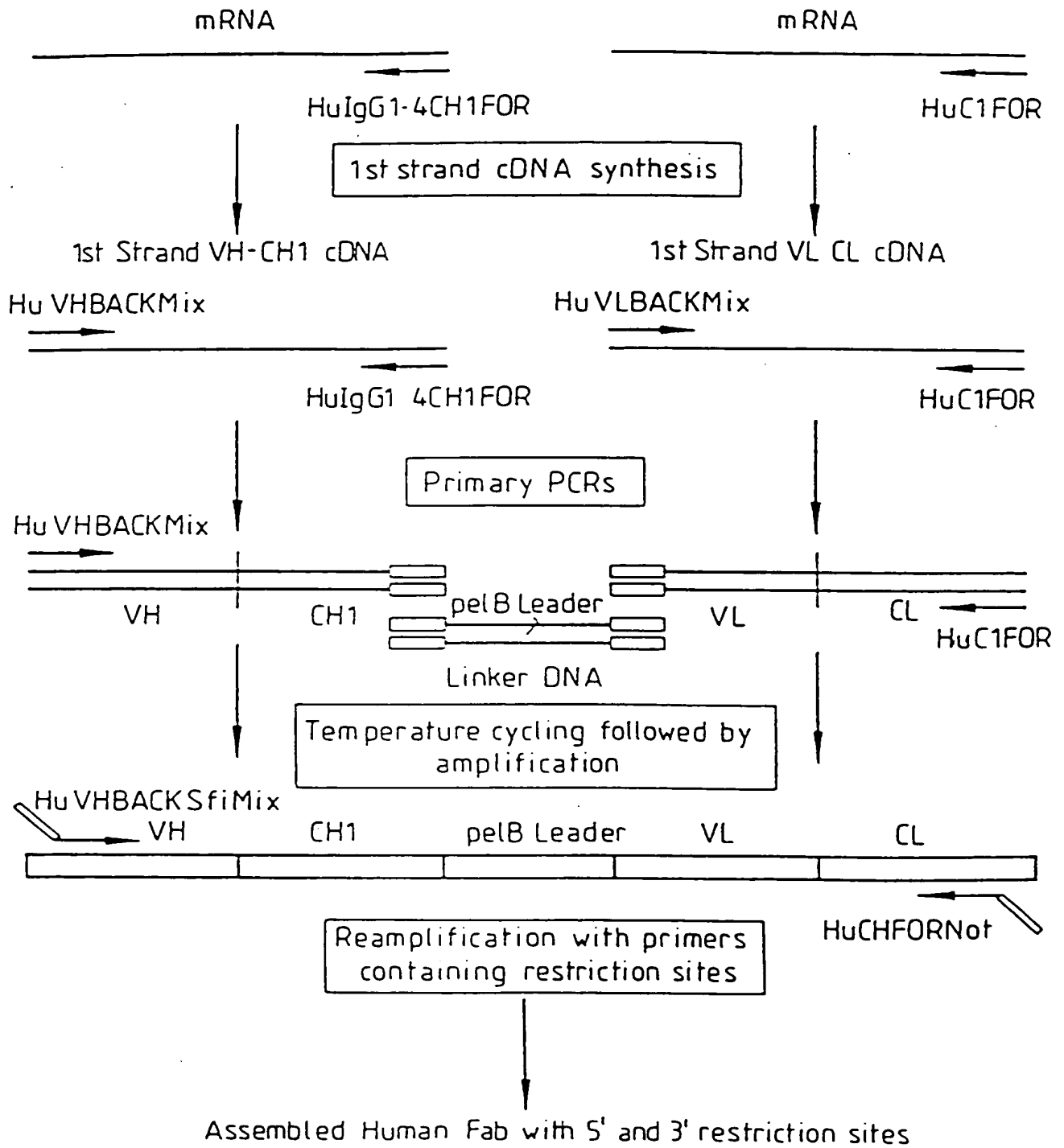


Fig.48(i)

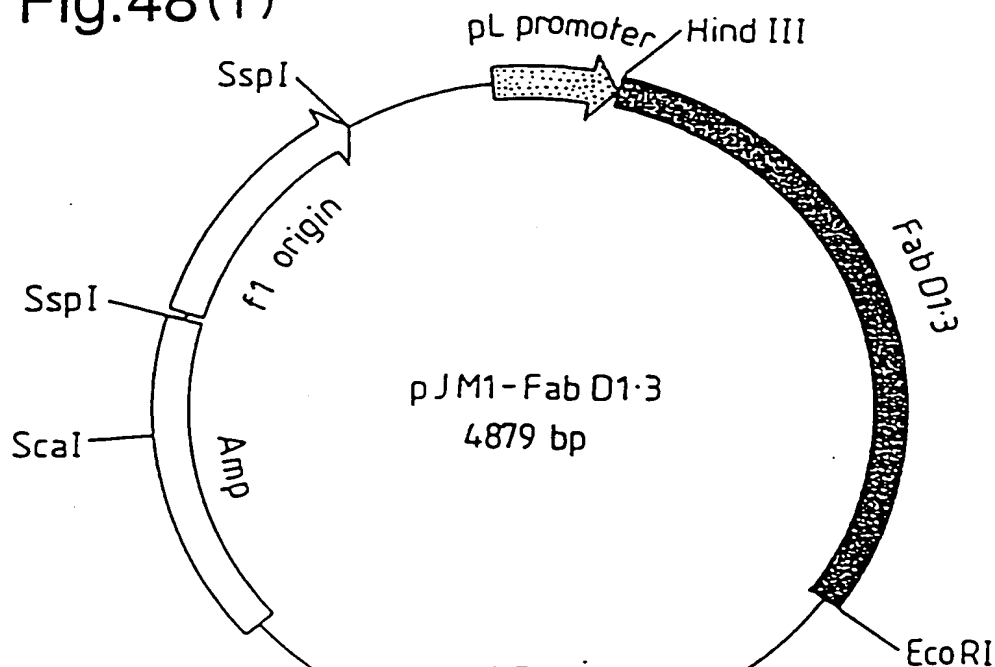


Fig.48(ii)

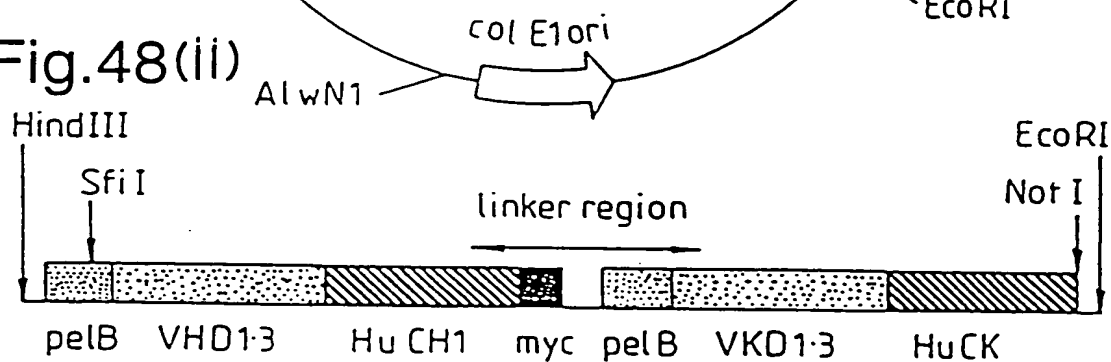


Fig.48(iii)

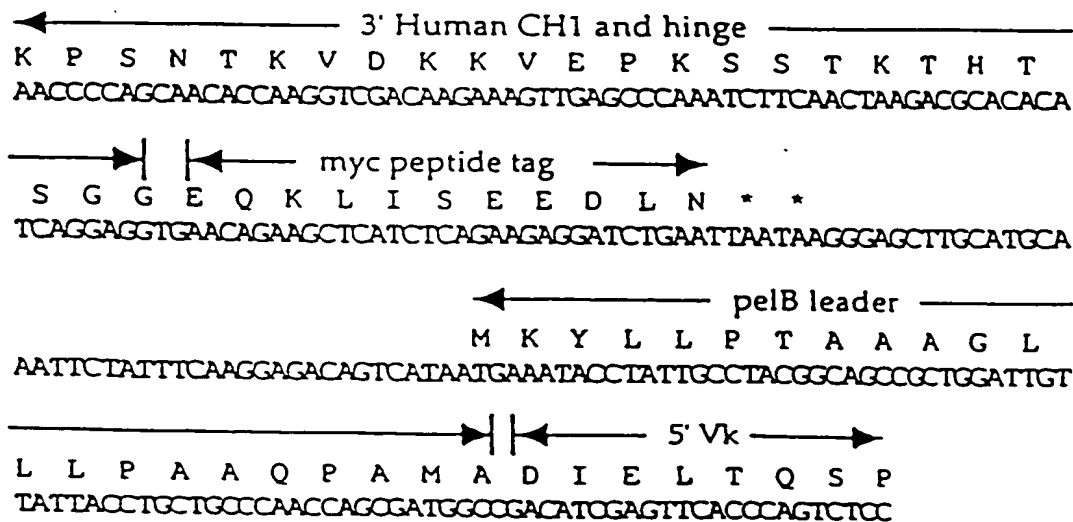


Fig.49.

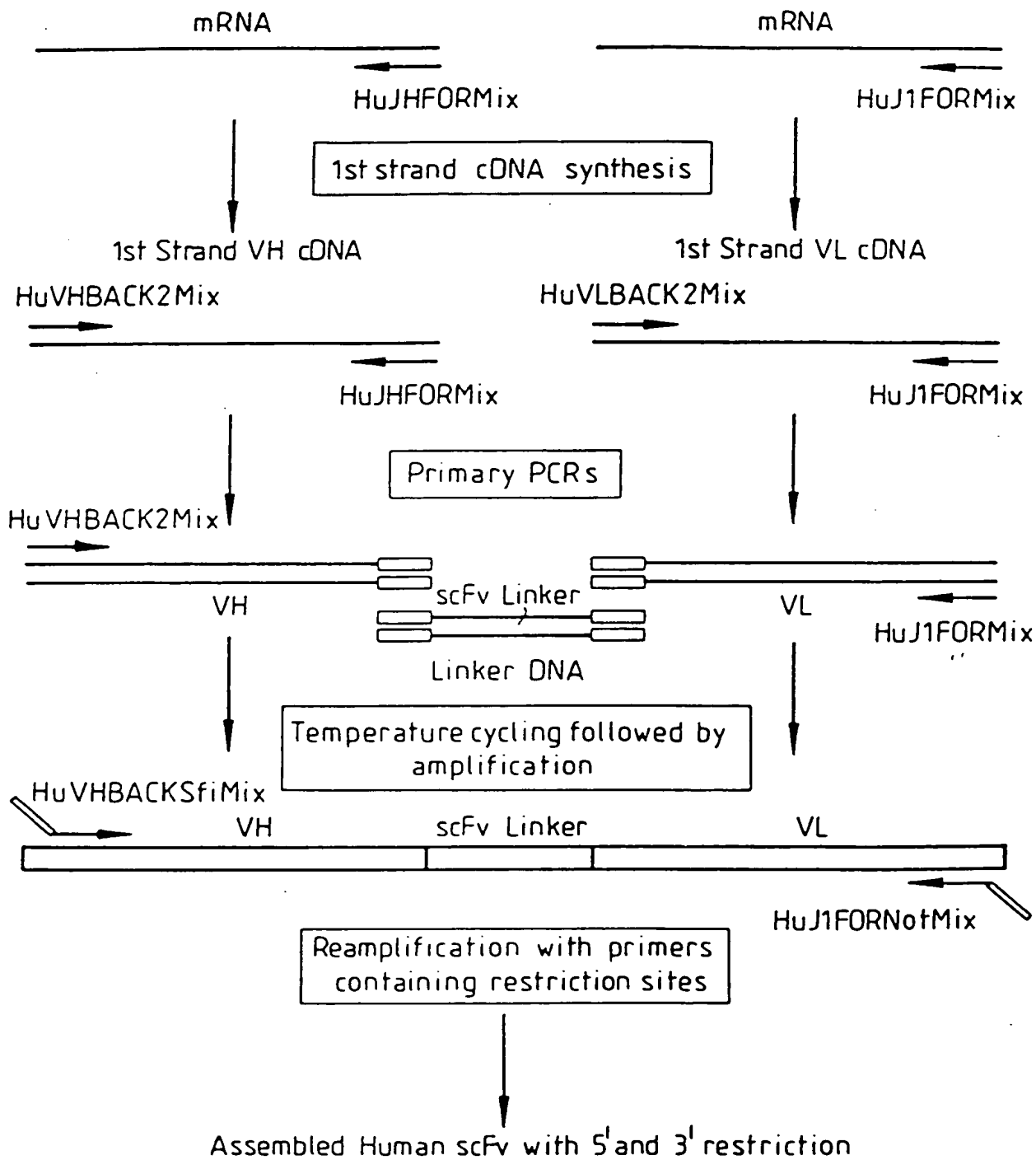


Fig.50(i)

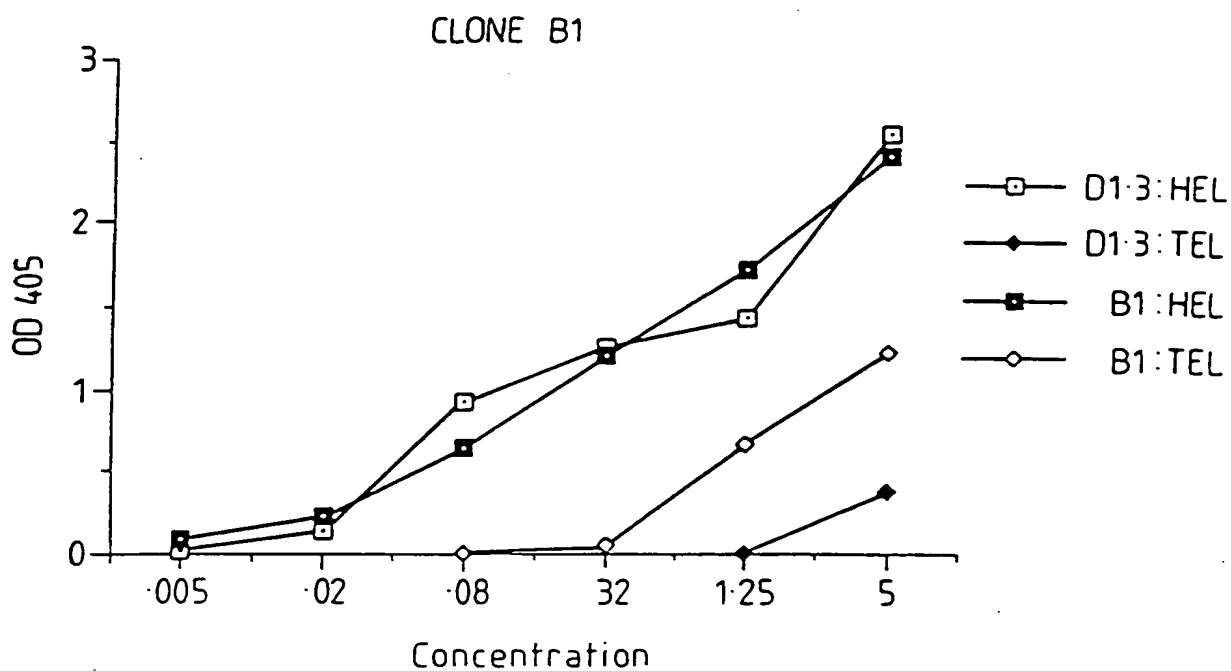
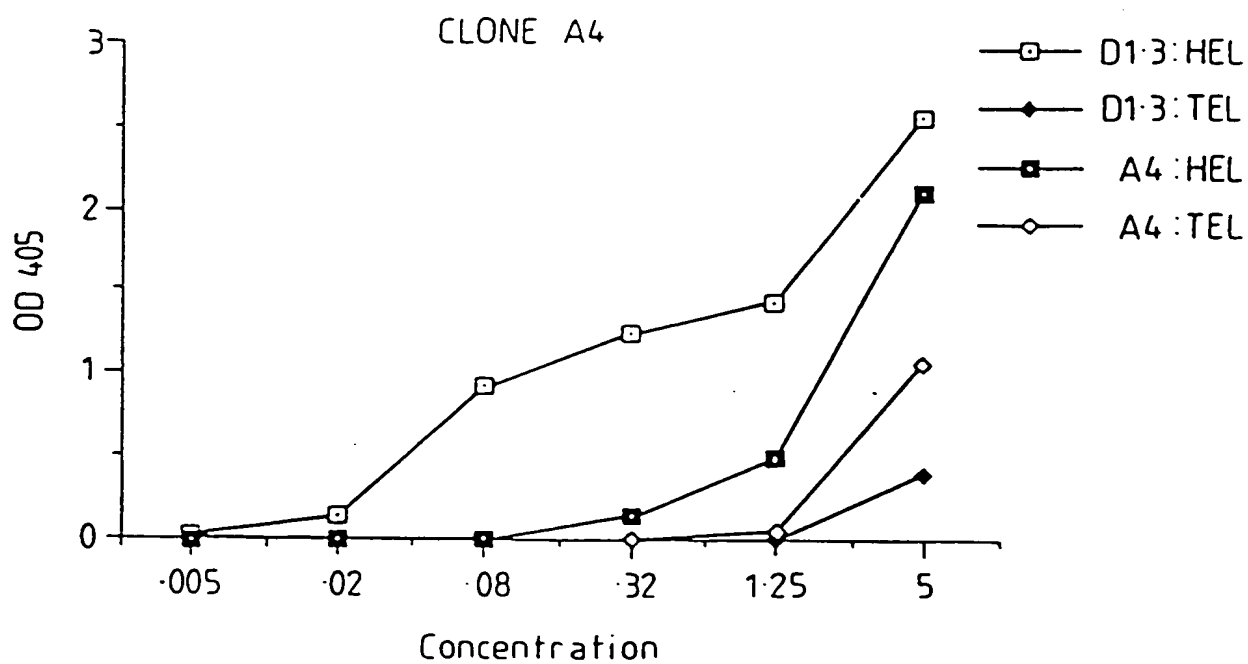


Fig.50(ii)



5541249-10393
5541249-10393

Fig.51.

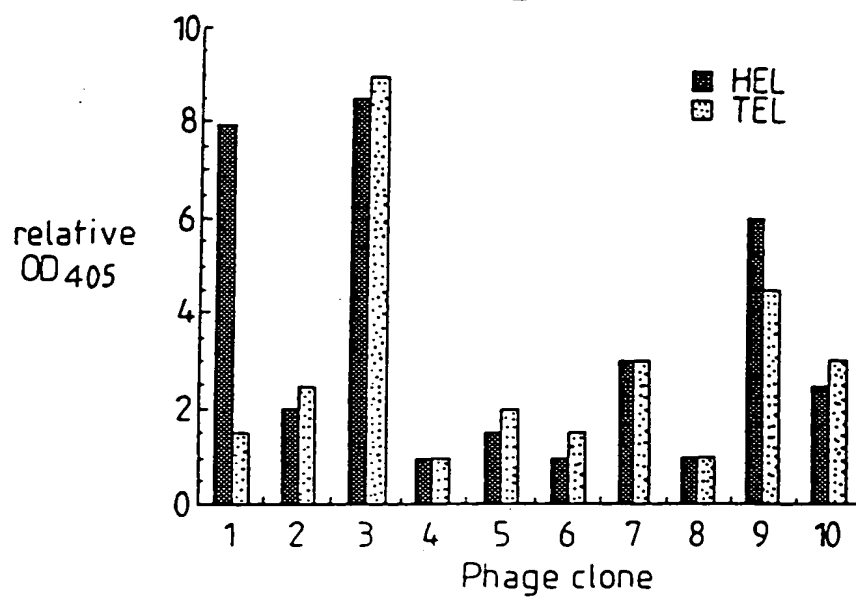


Fig.53.

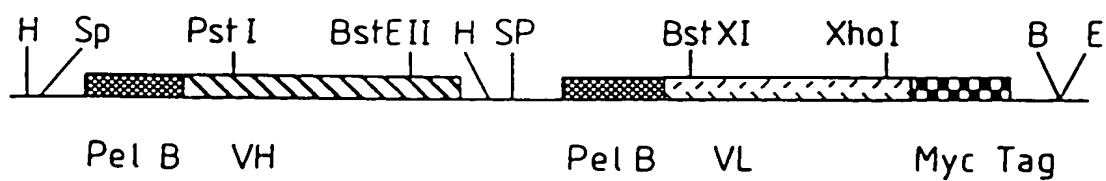


Fig.52.

CDR 1

CDR 2

D1.3 DIQMTQSPASLSASVGETVTITCRASGNIHNYLA WYQQKQKSPQLLVYYTTTLAD
M1F DIELTQSPSSLSASLGERVSLTCRASQDIGSSLN WLQQEPDGTIKRLIYATSSLDLS
M21 DIELTQSPALMAASPGEKVTITCSVSSSISSSNLHWYQQSETSPKPWIYGTSNLS

CDR 3

D1.3 GVPSRFGSGGTQYSLKINSLQPEDFGSYQCQHFWSPTPTFGGKLEIKR
M1F GVPKRFGSRGSDYSLTISSLESEDFVDYYCLQYA9SPWTFGGGKLELKR
M21 GVPVRFSGSGTSYSLTISSMEAEADAATYYCQWSSYPPLTFGAGTKLEIKR